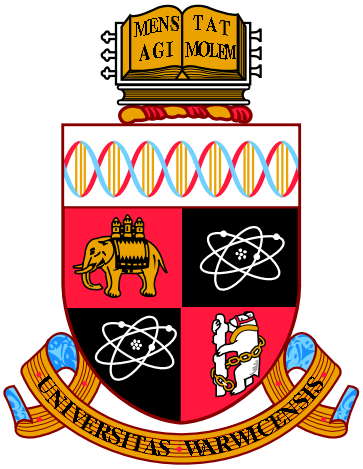

Ageing and Sleep in Human Balance and Falls: the Role of Wearable Sensors and Nonlinear Signal Analysis.

by

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Thesis

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Declarations

This thesis is submitted to the University of Warwick in support of my application for the degree of Doctor of Philosophy. It has been composed by myself and has not been submitted in any previous application for any degree.

The work presented (including data generated and data analysis) was carried out by the author except in the cases outlined below:

- The work presented in chapter 3 is a secondary analysis (meta-analysis) of previously published data. These data were extracted from 13 original articles, which are cited in this thesis.
- The work presented in chapter 4 is a secondary analysis of a public dataset, which was initially described by its authors in: Santos, D. A., & Duarte, M. (2016). A public data set of human balance evaluations. *PeerJ*, 4, e2648.

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2. Montesinos, L., Castaldo, R., & Pecchia, L. (2018). On the use of approximate entropy and sample entropy with centre of pressure time-series. *Journal of NeuroEngineering and Rehabilitation*, 15(1).

3. Montesinos, L., Castaldo, R., Cappuccio, F. P., & Pecchia, L. (2018). Day-to-day variations in sleep quality affect standing balance in healthy adults. *Scientific Reports*, 8(1), 17504.

Conference papers:

1. Montesinos, L., Castaldo, R., Piaggio, D., & Pecchia, L. (2018). Day-to-day variation in sleep quality and static balance: results from an exploratory study. In H. Eskola, O. Väisänen, J. Viik, & J. Hyttinen (Eds.), *EMBEC & NBC 2017. IFMBE Proceedings* (Vol. 65, pp. 611-614). Singapore: Springer Singapore.

2. Montesinos, L., Castaldo, R., & Pecchia, L. (2019). Selection of Entropy-Measure Parameters for Force Plate-Based Human Balance Evaluation. In L. Lhotska, L. Sukupova, I. Lacković, & G. S. Ibbott (Eds.), *World Congress on Medical Physics and Biomedical Engineering 2018. IFMBE Proceedings* (Vol. 68/2, pp. 315-319). Singapore: Springer Singapore.

3. Montesinos, L., Castaldo, R., & Pecchia, L. (in press). Promises and Challenges in the Use of Wearable Sensors and Nonlinear Signal Analysis for Balance and Fall Risk Assessment in Older Adults. *International Conference on Biomedical and Health Informatics 2019. IFMBE Proceedings.*

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Abstract

Wearable sensors and nonlinear signal analysis methods are empowering innovative ways of assessing balance and fall risk in older adults. However, their adoption in research and clinical practice creates new challenges. This thesis and the studies herein address some of these challenges and provide some insights concerning their optimal use.

Wearable inertial sensors offer the means for developing instrumented versions of clinical balance assessment tools, producing objective and accurate quantitative descriptors on the timing and execution of functional tasks. However, this research proves that selecting an adequate combination of sensor placement, movement task and the measured variable is crucial for discriminating subjects at a higher risk of falling. An optimal protocol for assessing fall risk based on wearable inertial sensors is identified and presented in this thesis.

Additionally, wearable devices offer the means for continuously monitoring physiological and behavioural variables, which can be used to infer outcomes linked to impaired balance and increased risk of falling in older adults. This research shows that wearable devices can be used to capture day-to-day variations in sleep quantity and quality, which in turn produce variations in balance. This situation can potentially expand the prevailing paradigm in fall prevention, from the current one focusing on the occasional assessment of risk factors and changes in the balance control system to a new one also including the continuous monitoring and detection of short-lived factors that might result in an imminent fall.

Finally, this research demonstrates that quantitative descriptors of nonlinear dynamics are more sensitive than linear measures to differences in balance control associated with ageing and risk of falling (e.g. non-fallers and fallers). The adequate selection of the input parameters required for the calculation of nonlinear measures is of paramount importance to achieve positive results. This thesis provides some recommendations for the parameter selection.

Collectively, the findings of this research confirm that wearable sensors and nonlinear signal analysis methods can improve and extend current tools and practices in balance and fall risk assessment.

Abbreviations

10MW test	10-Meters-Walking test.
ACF	Autocorrelation Function.
AF	Atrial Fibrillation.
ANOVA	Analysis of Variance.
ANS	Autonomic Nervous System.
AP	Anterior-Posterior.
ApEn	Approximate Entropy.
BBS	Berg Balance Scale.
BMI	Body Mass Index.
BoS	Base of Support.
BP	Blood Pressure.
CF	Eyes closed on a foam mat.
CI	Confidence Interval at 95%.
CNS	Central Nervous System.
	.
CoM	Centre of Mass.
CoP	Centre of Pressure.
CR	Eyes closed on a rigid surface.
CSD	Consensus Sleep Diary.
CV	Coefficient of Variation.
EC	Eyes Closed.
ECG	Electrocardiogram.
EEG	Electroencephalogram.
EMG	Electromyogram.

EO	Eyes Open.
EOG	Electrooculogram.
FES-I	Falls Efficacy Scale International.
FTSS test	Five-Times-Sit-to-Stand test.
HF	High-Frequency.
HR	Heart Rate.
HRV	Heart Rate Variability.
LF	Low-Frequency.
	.
Mini-BESTest	Mini-Balance Evaluation Systems Test.
ML	Medial-Lateral.
MSE	Multi-scale Entropy.
NREM	Non-Rapid Eye Movement.
OF	Eyes open on a foam mat.
OH	Orthostatic Hypotension.
OR	Eyes open on a rigid surface.
PD	Parkinson's disease.
PIM	Proportional Integrating Mode.
POMA	Performance-Oriented Mobility Assessment.
PPA	Physiological Profile Assessment.
PSG	Polysomnography.
PSQI	Pittsburgh Sleep Quality Index.
REM	Rapid Eye Movement.
RMS	Root Mean Square.
SampEn	Sample Entropy.
SD	Standard Deviation.
SE	Sleep Efficiency.
SOL	Sleep Onset Latency.

SSQ	Subjective Sleep Quality.
SWS	Slow Wave Sleep.
TAT	Time Above Threshold.
TBI	Traumatic Brain Injury.
TST	Total Sleep Time.
TUG test	Timed-Up-and-Go test.
	.
VLF	Very Low-Frequency.
WASO	Wake After Sleep Onset.
WHO	World Health Organization.
ZCM	Zero Crossing Mode.

Chapter 1

Introduction

1.1 Chapter overview

This chapter presents the use of wearable sensors and nonlinear signal analysis methods for assessing balance and fall risk in older adults, pinpointing the challenges that arise from their adoption in this field (section 1.2). Moreover, it introduces the research questions, aims and objectives of this work (section 1.3), as well as an overview of the research methods and tools used during this research (section 1.4). Finally, an outline of the thesis is provided (section 1.5).

1.2 Scope

Balance is an essential ability for successfully performing the activities of daily living. Even during seemingly simple activities such as standing and walking, complex regulatory mechanisms are required to preserve postural stability through the maintenance of the body's centre of mass within the limits of the base of support. Balance, a term describing the dynamics of body posture to prevent falling [1], arises from the complex interaction of sensory, motor and control systems (i.e. the balance control system). Briefly, visual, vestibular and proprioceptive information is integrated and processed by the cerebellum, basal ganglia and sensorimotor cortex, which in turn command the musculoskeletal system via the spinal cord and the peripheral innervation of muscles [2].

Impairment in any of these systems can result in a deficit in balance control. Such impairment may be due to the progressive decline of function in the course of healthy ageing, specific pathologies or behavioural factors [3, 4]. Balance impairment is common among adults aged 60 years and over (hereafter called older adults;

additionally, adults aged 18-59 are called younger adults), with estimates of its prevalence ranging between 20 and 50% [4].

Impaired balance control can ultimately result in a fall and have a profound impact on individuals regarding their quality of life and capacity for independent living. Falls are relatively common events among older adults. Approximately, 28 to 35% of community-dwelling older adults experience at least one fall each year [5]. The frequency of falls increases among older adults living in long-term care institutions, where 30 to 50% of them sustain a fall each year [6]. Older adults suffering from neurodegenerative diseases, such as Alzheimer's, Parkinson's and dementia, have higher prevalence of falls than their age-matched healthy counterparts [3]. Moreover, falls are the most frequent adverse event among hospitalised older adults, accounting for 32% of patient safety incidents in the United Kingdom [7]. In this age group, around 40 to 60% of falls lead to injuries, with 30 to 50% being minor injuries and at least 10% being serious injuries (e.g. hip fractures and head injuries) [5].

The high prevalence of balance impairments in older adults and their detrimental individual and societal impact has moved scores of researchers and clinicians to understand more about how balance control works, and how to quantify it at any point in time. Consequently, many balance and fall risk assessment tools have been developed, ranging from simple questionnaires, scales and functional mobility tests requiring no more than a stopwatch, to complex techniques relying on force-sensing platforms and optical motion capture systems, among other items of equipment [8]. To date, questionnaires and scales represent the preferred option in clinical settings, since they provide an inexpensive means for assessing functional performance of activities and movements which occur in the course of everyday life (e.g. stepping or walking) [4]. However, these tools are subjective (e.g. questionnaires) and provide no or limited information on the underlying cause of impaired standing balance (e.g. non-instrumented functional tests) [9]. On the other hand, instrumented techniques provide an objective assessment of balance control and produce large amounts of data which could potentially shed light on the underlying causes of balance impairments [8]. However, their cost and complexity of use have restricted their use in research and top-tier clinical settings.

The rise of wearable technologies is enabling novel ways of assessing balance and the risk of falling in older adults. In particular, wearable inertial sensors (i.e. micro-electronic devices integrating accelerometers and gyroscopes) represent a promising addition to clinical balance assessment tools. By producing detailed information on the timing and kinematics of functional tasks (e.g. walking), they

have the potential to provide an objective and accurate fall risk assessment. Some studies have made use of these sensors to produce instrumented versions of clinical balance assessment tools [10]. However, the variety of sensor placements, movement tasks and measured variables has precluded a consensus on their clinical relevance [11, 12]. Therefore, a systematic investigation of these factors to determine the optimal inertial sensor-based assessment protocol is relevant and timely.

Additionally, wearable technology is also enabling the continuous monitoring of physiological and behavioural variables (e.g. heart rate and sleep patterns, respectively), which can be used to infer health status and behaviours linked to impaired balance and increased risk of falling [13]. It can potentially expand the prevailing paradigm in fall prevention, from the current one focussing on the occasional assessment of risk factors and changes in the balance control system (e.g. reduction of visual acuity and lower-limb muscle strength), to a new one also including the continuous monitoring and detection of short-lived factors that might result in an imminent fall. Melillo *et al.* showed how wearable Electrocardiogram (ECG) sensors could be used to predict imminent falls due to standing hypotension, based on the analysis of ECG signals recorded five minutes before the subject got up from a chair [13]. Moreover, wearable technology offers new opportunities for in-home continuous sleep monitoring in the broader population [14, 15]. It is potentially relevant for fall prevention, given that poor sleep quality (i.e. sleep of short duration and increased fragmentation), both self-reported via paper-based scales and objectively-measured by actigraphy, is associated with future falls in older people [16–19]. Hence, if short-lived poor sleep quality has a similar effect on balance control, continuous sleep monitoring would be relevant for fall prevention programmes in frail populations and sleep disturbance-inducing scenarios (e.g. hospital wards). Therefore, the potential association between day-to-day variations in sleep quality and balance control deficits warrants further investigation.

The dissemination of dynamical systems theory and methods within the (bio)medical research community has inspired a new approach to the study of ageing and balance control in older adults [20]. Since the balance control system can be considered as a nonlinear system (i.e. reactions are not proportional to the applied stimuli), various quantitative descriptors of nonlinear dynamics have been proposed for the analysis of balance data (e.g. a time-series describing body sway during unperturbed standing). These descriptors can potentially provide further information on the underlying balance control mechanisms in ageing and represent more sensitive indicators of fall risk. Among these nonlinear measures, Approximate Entropy (ApEn) and Sample Entropy (SampEn) have been proposed as relative measures of

body sway regularity [8]. Relatively high entropy values suggest a more irregular body sway produced by control mechanisms that are too random to command balance properly. Conversely, relatively low entropy values suggest a more regular body sway produced by balance control mechanisms that are too stiff to cope with external factors demanding a flexible response [21]. The ability of ApEn and SampEn to discriminate between groups with different fall risk, and the adequate selection of the input parameters needed for their computation, have not been systematically investigated.

The ensemble of studies presented herein provides answers to some of the most pressing questions arising from the diffusion of wearable sensors and nonlinear signal analysis methods for balance and fall risk assessment, as well as for the study of the association between balance and short-lived factors.

1.3 Research questions, aim and objectives

The use of wearable sensors (e.g. inertial and physiological sensors) and nonlinear analysis methods has created unprecedented opportunities for the understanding of balance control and its assessment at any point in time, as well as for the ambulatory monitoring of health status and behaviours that are linked to impaired balance and fall risk. However, the adoption of these devices and methods has raised new questions. This research aims to identify how wearable sensors and nonlinear signal analysis methods can be applied to improve balance and fall risk assessment in older adults. In particular, the series of studies herein addressed the following research questions:

Research question 1: What is the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults, given the variety in sensor placements, movement tasks and measured variables that these devices allow?

Research question 2: Are quantitative descriptors of nonlinear dynamics more sensitive than linear measures to differences in balance control due to ageing and fall risk? If so, what is the optimal way to apply them (e.g. signal pre-processing, selection of input parameters)?

Research question 3: Are there any associations between day-to-day variations in sleep quantity and quality, monitored using wearable devices, and balance control?

Research question 4: What is the optimal method to capture variations in balance control due to day-to-day variations in sleep quantity and quality, linear or nonlinear measures?

The primary aim of this research was to advance the knowledge and methods related to the use of wearable sensors and nonlinear signal analysis for the assessment of balance and fall risk, both in research and clinical settings and in ambulatory monitoring of health status and behaviours linked to (impaired) balance.

Accordingly, the main objectives of this research are:

Objective 1: To identify the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults, including sensor placement, movement task and measured variable(s).

Objective 2: To determine whether quantitative descriptors of nonlinear dynamics are more sensitive than linear measures to differences in balance control due to ageing and fall risk.

Objective 3: To determine whether day-to-day variations in sleep quantity and quality, monitored using wearable devices, are associated with balance control variations.

Objective 4: To determine whether quantitative descriptors of nonlinear dynamics are more sensitive than linear measures to differences in balance control due to day-to-day variations in sleep quantity and quality.

In order to fulfil the objectives above, four different studies were designed and performed:

Study 1: A data set of 175 wearable inertial sensor-based measures extracted from 13 studies was analysed to identify the optimal sensor-based protocol for fall risk assessment in older adults.

Study 2: A public dataset of balance evaluations from 163 subjects was analysed to investigate whether nonlinear descriptors, in particular ApEn and SampEn, are more sensitive than linear measures to differences in balance control due to ageing and fall risk, and to identify the optimal way to apply them (e.g. signal pre-processing and selection of input parameters).

Study 3: A sample of 20 healthy subjects (age range: 21-40 years) underwent in-home sleep monitoring and balance assessment over two consecutive days, in order to investigate potential associations between day-to-day variations in sleep quantity and quality and balance in unperturbed standing.

Study 4: A sample of 31 healthy subjects (age range: 22-40 years) underwent in-home sleep monitoring and balance assessment over two consecutive days following an extended protocol, in order to investigate the sensitivity of nonlinear measures to differences in balance control in unperturbed standing due to day-to-day variations in sleep quantity and quality.

The fulfilment of these objectives required the application of a broad and diverse set of research methodologies, methods and tools for the collection and analysis of data, which are briefly introduced in the next section.

1.4 Overview of the research methods

In study 1, the potential use of wearable inertial sensors for assessing balance and fall risk in older adults was investigated (chapter 3). Some review articles on this topic have revealed high heterogeneity across the included studies concerning sensor placements, tasks and measured variables or features [11, 12]. This heterogeneity precludes a firm conclusion on the optimal sensor-based fall risk assessment protocol, making the translation of this technology from research laboratories to clinical settings difficult. This problem was tackled by performing a systematic review and meta-analysis of the previously published evidence. A systematic review aims to answer a research question by using explicit methods to identify, select, and critically appraise the relevant literature, in order to derive conclusions about that body of research [22]. Systematic reviews and meta-analyses are at the top level of the hierarchy of scientific evidence (Figure 1.1), since their outcomes represent a combination of the findings from all the studies pooled in the analysis [23]. Therefore, they are proven tools for decision-making in healthcare (e.g. to inform health technology assessment studies and clinical practice guidelines definition) [24].

In this research, static posturography was used extensively for assessing balance. This technique is one of the most popular in research and top-tier clinical settings [8, 25, 26], thus more data and evidence are publicly available. Static posturography entails the assessment of the body's Centre of Mass (CoM) or Centre of Pressure (CoP) motion during unperturbed standing [8]. CoM motion can be

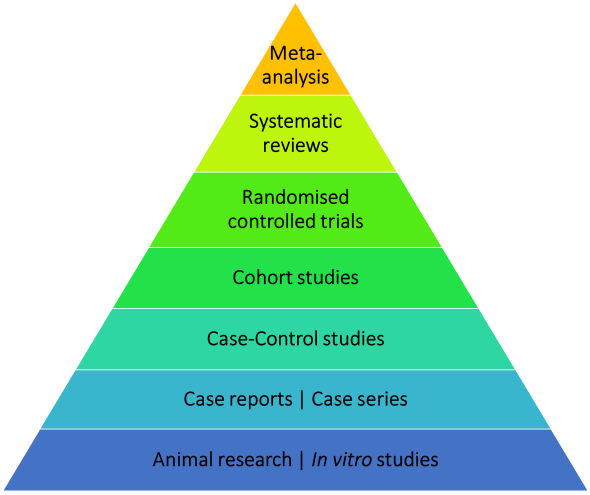

Figure 1.1: Hierarchy of evidence in (bio)medical research, where scientific evidence is ranked according to the strength of the freedom from various biases [23]. Meta-analysis is at the top, since this integrates the results of several independent studies. In contrast, animal research, *in-vitro* studies, case reports and case series are at the bottom. The studies presented in this thesis cover a diversity of designs, including a systematic review and meta-analysis (study 1), a cohort study (study 2) and two case-control studies (studies 3 and 4).

measured using inertial sensors or an optical motion capture system; CoP motion can be measured using in-shoe pressure sensors and force platforms [8]. Moreover, testing conditions can be manipulated to detect the deterioration of a specific sensory system (e.g. standing with eyes open and eyes closed for assessing changes in balance due to lack of vision). CoM and CoP motions are analysed using two approaches: global and structural analysis [8, 26]. In the first approach, the balance control system is assumed to have a linear nature and thus is characterised by general measures computed over the entire time-series, hence the name *global measures* [8, 26]. Among these measures are the range or amplitude of the signal and the mean and median frequency of its spectral components [8, 26]. In contrast, the second approach proposes that the balance control system must be considered a nonlinear system (i.e. its reactions are not proportional to the applied stimuli) [20]. Accordingly, nonlinear dynamic time-series analysis has been proposed as a tool to investigate its characteristics and mechanisms. In contrast to global measures, quantitative descriptors of nonlinear dynamics are sensitive to structural variations within time-series, hence they are often referred to as *structural measures* within the balance research community [8, 26].

In study 2, a public dataset containing CoP data for a cohort of 163 subjects

(both young and older adults) [27] was used to investigate whether quantitative descriptors of nonlinear dynamics are more sensitive than linear (global) measures to differences in balance control due to ageing and fall risk (chapter 4). Namely, ApEn and SampEn were used to quantify the regularity or self-similarity of CoP time-series by examining them for similar epochs or subseries: more frequent, similar subseries lead to lower entropy values. Thus low ApEn and SampEn values reflect a high degree of regularity or self-similarity [110, 111]. A relatively irregular body sway is produced by control mechanisms that are too random to command balance properly. In contrast, a relatively regular body sway is produced by balance control mechanisms that are too stiff to cope with external factors demanding a flexible response [21]. ApEn and SampEn were selected since they are suited to the analysis of noisy and short data (i.e. 100-5000 data points, with 1000 points used most often) [28, 110, 111].

In studies 3 and 4, cohorts of 20 and 31 healthy young adults (i.e. 21–40 years old, with seven subjects jointly involved in both studies), respectively, underwent in-home sleep monitoring and balance assessment over two consecutive days, in order to investigate the potential associations between day-to-day variations in sleep quantity and quality and balance in unperturbed standing (chapters 5 and 6). Sleep quality was selected as an exemplary case study to investigate the role of wearable devices for continuously monitoring health status and behaviours that are linked to impaired balance or fall risk. Sleep quality was chosen not only because there is evidence of an association between chronic poor sleep quality and disturbances, and impaired balance/fall risk [17–19], but also because an increasing number of consumer-grade wearable devices offer the possibility to track sleep on a regular basis [14, 15]. For balance assessment, CoP time-series were collected using a wearable in-shoe pressure-sensing system and a force platform (studies 3 and 4, respectively). These CoP time-series were later analysed by calculating some linear and nonlinear measures (studies 3 and 4, respectively). A baseline sleep assessment was performed using the Pittsburgh Sleep Quality Index (PSQI), a questionnaire that provides a global score for sleep quality over the past month [30]. Moreover, day-to-day variations in sleep quantity and quality were identified through a Consensus Sleep Diary (CSD) [31] and ascertained via actigraphy and Heart Rate Variability (HRV) analysis. Actigraphy, which is the measurement of body/limb movements based on acceleration signals, has gained popularity among sleep researchers and clinicians over the last years, since it allows tracking sleep under ecological conditions (e.g. at home) and for extended periods [32]. In contrast, Polysomnography (PSG), considered the "gold standard" for sleep studies, is generally conducted in a sleep

Table 1.1: Summary of studies performed during this research

Study	Design	Wearable technology	Signal analysis approach
1	Meta-analysis	Inertial sensors for fall risk assessment in standing and gait	Linear and nonlinear
2	Cohort	None	Linear and nonlinear
3	Case-Control	Physiological sensor for sleep monitoring, in-shoe pressure sensors for balance assessment in standing	Linear
4	Case-Control	Physiological sensor for sleep monitoring	Linear and nonlinear

laboratory and limited to one-night recordings [33, 34]. Moreover, HRV analysis has been put forward as a tool for assessing autonomic cardiac activity during sleep, providing clues about sleep architecture [35]. The concurrent use of actigraphy and HRV is opening up exciting possibilities for long-term, in-home monitoring and quantification of sleep based on wearable devices [36]. In this research, acceleration and ECG signals during sleep were collected using a wearable physiological sensor (described in chapter 5).

Table 1.1 presents a summary of the studies designed and performed in this research, specifying their type of design, as well as the methods and tools used for collecting and analysing the data.

1.5 Thesis outline

Chapter 1 presents the scope, research questions, aims and objectives of this thesis. Moreover, it presents an overview of the research methods and tools used during this work. Finally, it presents an outline of the thesis.

Chapter 2 introduces balance control and falls in older adults. This chapter presents the methods and techniques used to assess balance in older adults that are relevant to this thesis. Additionally, the chapter introduces the basic principles of sleep and highlights the methods for sleep assessment that were used in this research. Finally, it presents a discussion on the research gaps that were used to delineate the questions, aim and objectives behind the studies presented in later chapters.

Chapter 3 presents a systematic review and meta-analysis to identify the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults, including sensor placement, movement task and measured variables.

Chapter 4 presents the secondary analysis of a public dataset of CoP time-series performed to investigate whether nonlinear descriptors, in particular ApEn and SampEn, are more sensitive than linear measures to differences in balance control due to ageing and fall risk, as well as identifying the optimal way to apply them (e.g. signal pre-processing, selection of input parameters).

Chapter 5 presents an experimental study conducted on a cohort of 20 healthy subjects in order to investigate potential associations between wearable sensor-ascertained day-to-day variations in sleep quantity and quality, and balance in unperturbed standing.

Chapter 6 presents an experimental study conducted on a cohort of 31 healthy subjects in order to further investigate the associations between day-to-day variations in sleep and balance, as well as the sensitivity of nonlinear measures, in particular ApEn and SampEn, to differences in balance control due to daily variations in sleep quantity and quality.

Chapter 7 summarises the main conclusions presented in this thesis and provides some recommendations for further work based on the identified limitations and opportunities.

Chapter 2

Background

2.1 Chapter overview

Balance emerges from the complex interaction of sensory, motor and control systems, making up the balance control system. Section 2.2 presents the basic principles of balance control in older adults, including a description of the systems involved in balance during standing and walking.

Falls are one of the most prevalent and severe consequences of balance deficits in older age. Section 2.3 presents some data concerning the prevalence of falls and fall-related injuries in older adults, as well as their economic impact on healthcare systems. More importantly, this section introduces the risk factors for falls in older adults.

Various methods and techniques to assess balance in older adults have been proposed, both non-instrumented and instrumented. Section 2.4 presents the methods that are most relevant to this research, including the use of wearable inertial sensors and nonlinear signal analysis algorithms.

Sleep of short duration and poor quality is associated with falls in older adults. Nevertheless, it has not received as much attention as other risk factors, even though sleep alterations are prevalent during older age. Section 2.5 introduces the basic principles of sleep, including a brief description of the normal sleep architecture and the changes it experiences with ageing. In addition, this section presents the methods and techniques for sleep assessment, emphasising on those that are relevant for this research.

A critical appraisal of the sections above reveals some gaps in the body of knowledge concerning the use of wearable sensors and nonlinear signal analysis methods for the assessment of balance and fall risk in older adults. This chap-

ter concludes with a summary of its contents, pinpointing the research gaps that were identified and used to delineate the aims and objectives underlying the studies presented in chapters 3 to 6 (section 2.6).

2.2 Balance control in older adults

2.2.1 The balance control system

Balance control has been defined as the control of the body's Centre of Mass (CoM) relative to the Base of Support (BoS) [2]. Humans' upright posture requires an active balance control in order to counteract the effects of gravity, which tends to move the CoM out of the BoS. In a static condition, such as unperturbed bipedal standing, the CoM has to be continually moved to maintain it within the limits of the BoS (i.e. the convex polygon defined by the lateral borders of the feet, whose area has been estimated at 829±103 cm^2 in a sample of 13 healthy adults) [26, 37]. This constant movement of the CoM during standing is called postural sway, with older adults (≥60 years old) showing generally larger postural sways than young adults (18–59 years old) (Figure 2.1). In a dynamic condition, such as perturbed standing and walking, the CoM can be momentarily out of the BoS, but it has to be moved back to within the BoS, or the BoS must be enlarged to avoid falling. Two strategies are available to the balance control system in order to adjust the position of the CoM [38]. When, in standing, small or no perturbations exist, the muscles around the ankle joint can be activated to produce a torque and accelerate the CoM around the ankles in the desired direction. Otherwise, movements of some body parts can counteract the effects of the perturbation by accelerating the CoM in the opposite direction (for instance, by moving the arms backwards after being pushed forwards). In more dynamic situations, the BoS can be moved by stepping or enlarged by grabbing for hand support [2].

To activate the muscles to move the CoM in an appropriate direction or to reconfigure the BoS if required, the Central Nervous System (CNS) requires information on the present position and acceleration of the CoM [1]. This information is provided by different sensory modalities and is essential for balance control. The human balance control system is thus made up of the sensory, central nervous and motor systems (Figure 2.2). The sensory system assesses the current position of the CoM in relation to the BoS, as well as the overall body posture in relation to the environment. The CNS weights the sensory information, decides on actions required to maintain or recover balance, and activates muscles accordingly. The motor system performs the required mechanical actions and the result is measured again

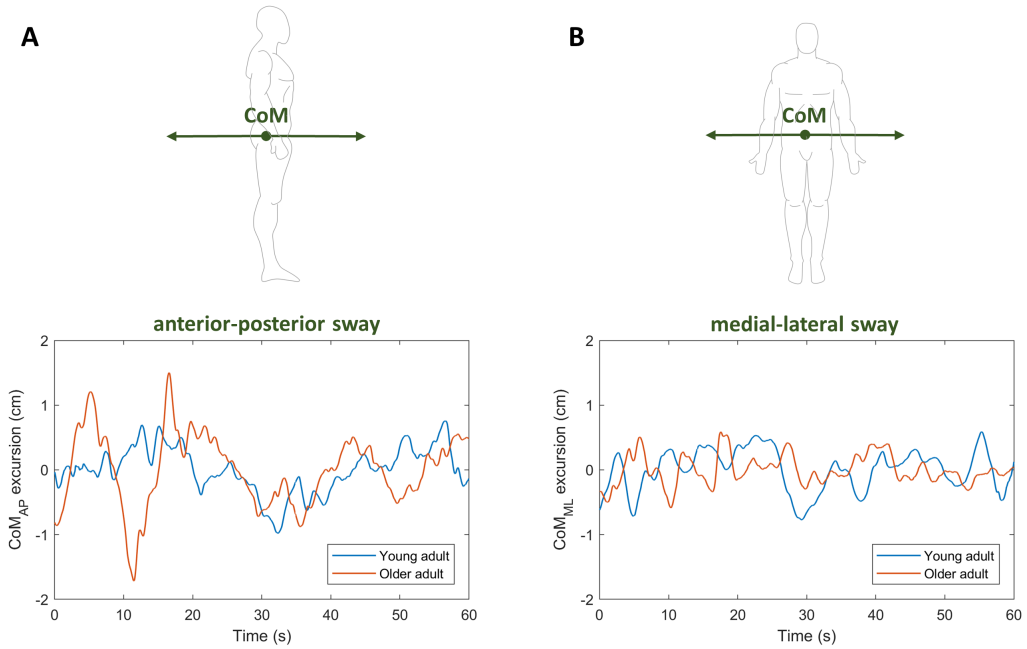

Figure 2.1: Postural sway during standing. Illustration of the continuous movement of the body's centre of mass (CoM) in the **(A)** anterior-posterior (AP) and **(B)** medial-lateral (ML) axes. For comparison, the CoM excursions are shown for a young adult (25 years old) and an older adult (70 years old). Data sourced from a public dataset [27].

by the sensory system. This sequence of steps defines the feedback mechanisms of balance control. Alternatively, anticipatory or feedforward control mechanisms can also be used to maintain balance. Sensory information can be used to predict imminent perturbations and pre-emptive action can be taken to attenuate or even avoid a perturbation (for instance, a rugby player widening his BoS in anticipation of an expected frontal impact with a player of the opposite team).

The building blocks of the balance control system are described more extensively in the next subsections.

2.2.1.1 The sensory system

Sensory information required for balance control is generated by the vestibular, visual, and somatosensory systems (Figure 2.2).

The *vestibular system* comprises the semicircular canals and the otoliths, which are localised in the head behind the ears (that is, under the mastoid processes). The otoliths measure linear accelerations of the head, providing informa-

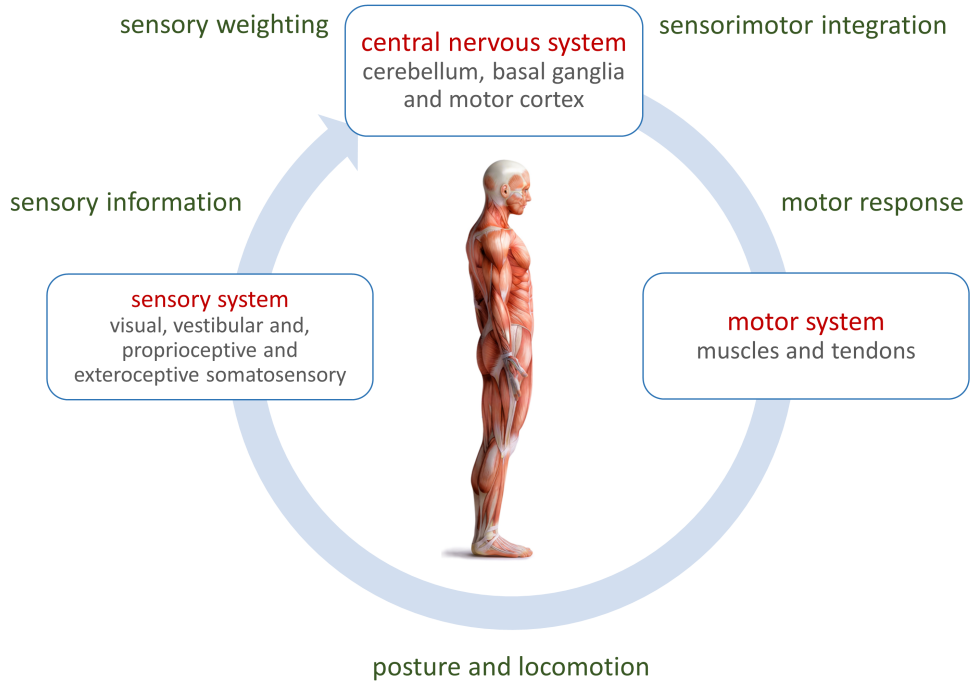

Figure 2.2: Balance control feedback loop. The sensor system provides information to the central nervous system. The central nervous system weights and integrates information from the different sensory modalities and generates motor responses to activate the muscles to adapt posture or movements to maintain balance. Adapted from the literature [2].

tion about its orientation relative to the vertical. The semicircular canals measure angular accelerations, providing information on the rotational movements of the head. Adequate functioning of these organs is essential in order to maintain visual fixation during head movements and stabilise the head during movements of the trunk and extremities [4]. The importance of the vestibular system for maintaining vertical postures can be experimentally demonstrated by electrical stimulation of the vestibular organs. A bipolar current applied behind the ears during standing alters the firing rate of the peripheral nerves connecting the vestibular system to the brain, which in turn causes an illusion of sway towards the side of the cathode, eliciting sway in the opposite direction [39].

The *visual system* transforms light patterns on the retina into images of the environment. These images provide essential information for balance control, including: 1) an estimate of the vertical; 2) the orientation of the head relative to the vertical; 3) the rotational movements of the head; and, 4) a spatial map of

the environment in which objects are assessed in terms of their location, direction and speed of movement [2, 4]. The latter is essential for anticipation of potential balance threats. Several studies have confirmed the importance of visual information for balance control, made apparent from the increase in postural sway observed in standing with eyes closed compared to standing with eyes open [40].

The *proprioceptive somatosensory system* comprises the muscle spindles, Golgi tendon organs, and joint and skin receptors, distributed over the whole body [41]. These sensors provide information used to assess the orientation and movement of body segments relative to each other [2]. Muscle spindles are the primary source of proprioceptive information since they encode variations in muscle length and the speed of those variations.

The *exteroceptive somatosensory system* comprises a set of receptors in the soles that measure skin strain, thus providing information on the forces acting on the feet base. The importance of these receptors for balance control can also be experimentally demonstrated by electrical stimulation of the soles, which normally elicits an increase in postural sway [2].

2.2.1.2 The central nervous system

At its most basic level, balance control relies on automated responses generated by the brain stem, expressed by the simultaneous activation of muscles around several joints [2]. However, more complex balance responses require the involvement of higher centres of the brain to integrate different sources of sensory information and command motor responses accordingly. The centres of the brain that have been linked to posture control are the cerebellum, the basal ganglia and the cortex [42].

The *cerebellum* plays an essential role in balance control. The scientific evidence suggests that it integrates sensory information concerning the body and the environment, thus enabling fine-tuning motor activity generated to maintain and restore balance [43]. The importance of the cerebellum for balance control has been observed in studies on humans and other animals [44]. Patients with cerebellar lesions exhibit severe balance disorders, which they frequently compensate for with a wide stance to enlarge the BoS. Recent evidence also suggests that the cerebellum is involved in the generation of appropriate patterns of limb movements, dynamic regulation of balance, and adaptation of posture and locomotion through practice [44].

The *basal ganglia*, a group of subcortical nuclei in the brain, are primarily involved in motor control [45]. People with basal ganglia lesions (e.g. Parkinson's disease patients) display resting tremor, stiffening and bradykinesia (i.e. the extreme

slowness of movements and reflexes), which compromise their ability to cope with balance perturbations [42]. The basal ganglia also play a part in sensory integration and weighing [45].

The role of the *cortex* in balance control is still debated. Yet, there is some evidence suggesting that the premotor and primary motor cortices play a role in anticipatory postural adjustments [46]. Cortical activity in the left premotor area has also been associated with balance control in unperturbed gait [47]. Impaired balance in gait has also been observed when subjects are simultaneously performing a demanding cognitive task, which speaks about the importance of the cortex for balance control [2].

2.2.1.3 The motor system

Muscles and *tendons* are the most relevant elements of the motor part of the balance control system [2]. In unperturbed standing, a moderate but continuous and accurate force production is required to maintain the body's CoM over the BoS. Yet, rapid and vigorous contractions of group muscles in the lower limbs, trunk and even upper limbs are required to compensate for large balance perturbations. The calf and hip abductor muscles are crucial for balance control during standing and gait [1, 48]. Moreover, tendon stiffness largely determines the rate at which forces are transferred to the skeleton and hence at which movements can be controlled [2].

2.2.2 Balance control in unperturbed standing

Balance control requires controlling the position of the body CoM relative to the BoS. In unperturbed bipedal standing, the CoM lies approximately anterior to the second sacral vertebra, and the BoS is formed by the lateral borders of the feet [26]. In this posture, the force of gravity produces a torque around the ankle joints. Active control of balance is needed to counteract this gravitational torque and thus to avoid falling [2]. Balance control is achieved by activating the muscles around the ankle joint in order to produce a counteractive torque around the ankles, a mechanism known as the *ankle strategy*. When the ankle muscles cannot act, hip muscles are activated in order to move the CoM posteriorly or anteriorly, a mechanism known as the *hip strategy* [1]. As a result of the interplay of the gravitational force and the postural adjustments produced by the balance control system, the body sways continuously, and thus the CoM moves over the BoS (Figure 2.1). In unperturbed standing, the CoM moves over the central part of the BoS [26].

The magnitude of CoM excursions (also know as body or postural sway)

is often used as a measure of the integrity of the balance control system and is associated with several factors [2]. First, there are age effects on the amplitude of postural sway: older adults generally show wider CoM excursions than young adults. The amount and quality of sensory information available to the balance control system at any given moment also affect body sway. The amplitude of CoM excursions tends to increase in both young and older adults when they stand still with Eyes Closed (EC) compared to the amplitude when they stand with Eyes Open (EO), yet, the increase is generally more substantial for older adults [2]. This is also the case when exteroception is perturbed, for instance, by standing on a compliant surface (e.g. a foam mat). Figure 2.3 illustrates this phenomenon by showing the CoM excursions for a young adult and an older adult during standing on a rigid surface and a foam mat with EO [2]. All in all, the scientific evidence suggests that older adults are less resilient to perturbations of any of the sensory modalities involved in balance control. Yet, sometimes older adults show narrower postural sways than young adults [2], possibly because in some situations older adults manage to control balance by adopting a more rigid stance [2].

The ability to control balance is also challenged by exerting perturbations on the CNS, particularly in older adults [2]. This phenomenon has been observed in experiments in which the participants perform a cognitive task (e.g. counting down from 100 by 7) while simultaneously standing still. In this situation, the performance in the cognitive task or balance control is more affected in older adults than in young adults [49]. This is possibly explained by the involvement of the cortex in balance control mentioned earlier. Moreover, an association between cognitive abilities and balance control in unperturbed standing has also been found [50]. The relationship between cognition and balance control is more evident in older adults with dementia, who suffer from severe losses of balance more frequently that their cognitively intact counterparts [4].

Finally, the status of the motor system can also influence balance control in unperturbed standing. Muscle strength determines the time that older adults can maintain balance in an upright posture [51] and a lower precision in the production of muscle force is associated with wider postural sways [52].

2.2.3 Balance control in unperturbed gait

During unperturbed gait, the body's CoM is voluntarily moved forward, at which point the BoS has to be displaced to prevent falling. This reconfiguration of the BoS during walking is achieved by actively controlling the legs' swing in an accurate and coordinated manner in order to deal with variations in the environment (e.g.

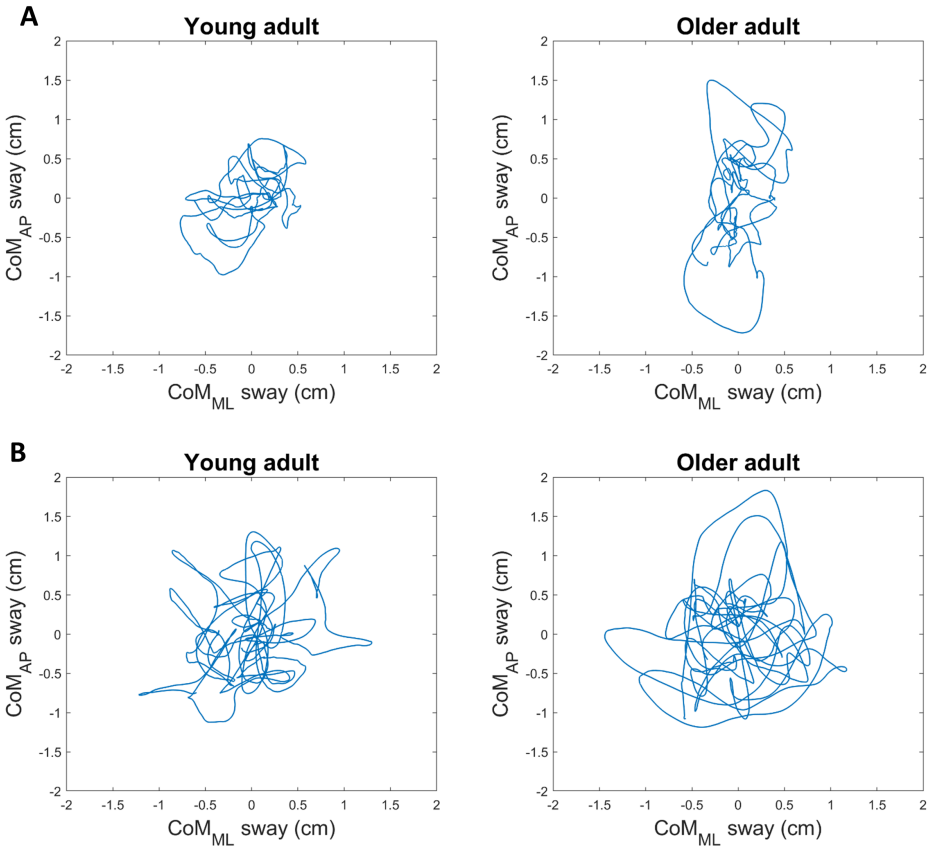

Figure 2.3: Bidirectional postural sway during bipedal standing. Body centre of mass trajectories for a young adult (25 years old) and an older adult (70 years old) during quiet standing **(A)** on a rigid surface, and **(B)** on a foam mat. Data sourced from a public dataset [27].

different types of surface). Moreover, the control of balance in the Medial-Lateral (ML) direction is more challenging than it is in unperturbed standing [2].

Several quantitative descriptors have been developed to characterise unperturbed gait. A first approach looks at average values of time and spatial measures of the gait cycle and its different stages (e.g. step time, length and width) [53]. Older adults tend to walk with wider steps than young adults. Wider steps are seemingly a strategy older adults take to increase their BoS. However, wider steps produce wider and faster CoM movements in the ML direction, which can jeopardise balance in cases when environmental conditions require a narrower step width [2].

A second approach to the assessment of gait relies on the notion that unperturbed gait is a periodical sequence of movements with a mostly regular and

stable behaviour. Accordingly, gait measures used in this approach quantify the variability and stability of gait, which are then used to study how these measures vary across age and fall risk status groups [54–56]. Older adults, particularly those with higher fall risk, show generally more substantial variability and lower stability in gait [54–56].

Gait variability and stability are linked to muscle strength [2]. Moreover, narrower step widths are associated with degenerative changes in the brain in older adults, suggesting that impaired brain connectivity prevents them from compensating their balance impairments with an increase in the BoS [2].

2.3 Falls in older adults

2.3.1 Definition

Falls have been defined by the World Health Organization as "an event which results in a person coming to rest inadvertently on the ground or floor or other lower level [57]." Similarly, the Prevention of Falls Network Europe have defined a fall as "an unexpected event in which the participant comes to rest on the ground, floor, or lower level [58]." Some other definitions have been coined using more specific terms as an attempt to differentiate falls caused by perturbations to the balance control system (accidental falls) from those produced by specific threatening events or medical conditions (non-accidental falls). For instance, the Kellogg International Working Group on the prevention of falls in senior citizens defined a fall as "unintentionally coming to the ground or some lower level and other than as a consequence of sustaining a violent blow, loss of consciousness, sudden onset of paralysis as in stroke or epileptic seizure [59]."

2.3.2 Impact

Falls are a leading cause of injury and death among older adults and a significant public health issue [5, 7, 60]. Thirty-three per cent of the community-dwelling adults over the age of 65 experiences a fall every year [61], with this figure increasing to 50% for those over the age of 80 [62]. The frequency of falls increases among older adults living in long-term care institutions, where 30 to 50% of them sustain a fall each year [6]. Older adults suffering from neurodegenerative diseases, such as Alzheimer's, Parkinson's and dementia, have higher prevalence of falls than their age-matched healthy counterparts [3]. Moreover, falls are the most frequent adverse event among hospitalised older adults, accounting for 32% of patient safety incidents

in the United Kingdom [7].

About 30 to 50% of falls lead to minor injuries, such as bruises or lacerations. However, 5 to 10% of falls result in major injuries, such as fractures and Traumatic Brain Injury (TBI) [63, 64]. Falls account for 90% of all hip fractures and 46% of deaths in TBI patients [3, 63]. Furthermore, about 50% of older adults who fall are unable to get up by themselves after the event. Hence, those who fall in private spaces (e.g. their own houses) often remain on the ground for a long time, which leads to further issues, such as dehydration, pressure sores, rhabdomyolysis and pneumonia [65].

Besides, 40% of older adults who fall have their activities of daily living restricted after the initial event, since they develop a marked fear of falling once again [66]. Their restrained activity leads to a decline in physical fitness, isolation and depression, which in turn increases the risk of further falls [66].

Falls also have a sizeable impact in terms of costs for healthcare systems and society. In the United Kingdom alone, the annual cost to the National Health Service (NHS) has been estimated at £2.3 billion per year [67]. Moreover, falls lead to indirect costs, such as the loss of productivity of family members and other caregivers. The average lost earnings due to falls could approximate £30,000 per annum for the United Kingdom [6].

2.3.3 Risk factors and other associations

A risk factor is defined as "any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury [68]." In the context of falls, a risk factor is the presence of a condition which, due to its direct impact on the balance control system, leads to an increased risk of falling. On the other hand, an association is a statistically significant correlation between a condition and a fall, without a direct causal relationship between the associated factor and falling.

Risk factors for falls are usually categorised into intrinsic and extrinsic [3]. Intrinsic risk factors comprise age-related changes to the balance control system, specific medical conditions and behavioural factors. Extrinsic risk factors comprise fall hazards in and around the home, as well as inadequate footwear. Intrinsic and extrinsic risk factors for falls are summarised in table 2.1 and described in detail below.

Table 2.1: Risk factors for falls in older adults [3]. Intrinsic risk factors include age-related changes in any of the sensory, neural or motor systems involved in balance control, some specific medical conditions and health-related behaviours. Extrinsic risk factors include the footwear used by the person and some elements in the environment, especially at home.

Intrinsic risk factors	
Age-related changes	Sensory system
	Central nervous system
	Motor system
Medical conditions	Neurological/Neurodegenerative problems
	Cardiovascular problems
	Visual problems
	Osteoarthritis
	Urinary incontinence
	Cognitive and mental factors
Behavioural factors	Use of medication
	Sleep quantity and quality
Extrinsic risk factors	
Home environment	Poor lighting
	Slippery surfaces
	Loose rugs
Footwear	Use of slippers

2.3.3.1 Intrinsic risk factors

Age-related changes. Balance control requires the integration of the sensory, nervous and motor systems. Adequate functioning of these systems declines with age, increasing fall risk. This decline in function is observed even in the absence of disease. Many older people with a history of falls have no identifiable neurological or musculoskeletal disease, yet perform poorly in tests of sensorimotor function [69].

Impaired sensory function produces inaccurate and conflicting sensory information about body posture. The decline of the nervous system results in abnormal sensory weighting and sensorimotor integration, producing imprecise corrective responses to perturbations of balance. Impaired motor function hinders the execution of these corrective responses.

Age-related changes to the balance control system are listed and described below.

1. Sensory system. Healthy ageing is accompanied by changes in the sensory

subsystems involved in balance control, which are briefly described below. Also, with ageing the nerve connections from the sensory system to the CNS lose fibres and myelin coatings, leading to a reduction in nerve conduction, thus slowing down feedback responses for controlling balance [70].

(a) Vestibular system. Healthy ageing is accompanied by a loss of sensors in the vestibular organs, reflected in lower amplitudes of responses elicited by vestibular electrical stimulation [2]. Besides, the prevalence of vestibular pathologies increases from around 50% in the 7th decade to 85% in the 9th decade of age [71]. Vestibular disorders increase fall risk, yet it is not yet clear whether reduced vestibular function in healthy, older adults also has this effect [72].

(b) Visual system. A progressive decline in vision (i.e. visual acuity, depth perception, contrast and glare sensitivity, and dark adaptation) starts around the age of 50 [72]. Yet, after the age of 60, the improvement in visual acuity provided by prescription lenses decreases [73]. Impaired depth perception is considered one of the strongest risk factors for multiple falls in community-dwelling older adults [74]. The likelihood of tripping over obstacles, such as steps, edges and cracks in the footpath increases with a loss of contrast sensitivity [72].

(c) Proprioceptive and exteroceptive somatosensory systems. The number and sensitivity of muscle spindles and skin receptors in the foot soles decrease with ageing. Older women show 3 to 4 times higher threshold for the detection of movement in the ankle than young women [75]. Reductions in acuity of posture and movement perception of the knee, ankle and big toe are associated with a higher fall risk [70].

2. Central nervous system. Healthy ageing is accompanied by a loss of brain cells and neural connections, with the prefrontal cortex and the cerebellum suffering the most and least prominent losses, respectively. These losses lead to a decreased ability to integrate sensory information, making older adults more sensitive to sensory perturbations [2]. These brain changes are associated with impaired balance control and increased fall risk [49].

3. Motor system. Healthy ageing is accompanied by a progressive decrease in muscle mass, which results in a decline of muscle strength [4]. Muscle weakness of the lower limbs is highly correlated with fall risk in older adults, while muscle strengthening exercise interventions improve balance control [4]. Muscle power also decreases with age, due to changes in the contractile properties

of muscle fibres and a decreased stiffness of tendons. As a result, older adults are limited mainly in performing fast dynamic movement tasks, and thus often less successful in regaining their balance after tripping over an obstacle than young adults [2].

Medical conditions. Frail, older adults with multiple chronic illnesses experience higher rates of falls than their more active, healthier counterparts [76]. This is so because many falls occur as a result of specific, identifiable medical conditions. These medical conditions are listed below.

1. Neurological and neurodegenerative problems
   (a) Stroke. After a stroke, many people are unable to produce enough muscle force in lower limbs and to coordinate the activation of different muscle groups. Cerebrovascular accidents are common in older adults and are associated with a two to sixfold increase in fall risk [77].
   (b) Vestibular pathologies, such as Menière's disease, produce obvious balance impairments in standing and gait. These pathologies are reflected in larger body sways and increased BoS during standing, as well as in unsteady gait patterns. Vestibular pathologies are also the most frequent cause of persistent and recurrent symptoms of dizziness often reported by older adults [77].
   (c) Peripheral neuropathy can result from diabetes mellitus, alcohol abuse, vitamin B12 deficiency and chemotherapy, among others [77]. Peripheral neuropathy affects proprioception, thus impairing balance. Peripheral neuropathy is associated with a higher fall risk [77].
   (d) Parkinson's disease (PD) patients show tremor, extreme slowness of movements and reflexes, and muscular rigidity. Many people suffering from PD experience frequent falls, due to their rigid posture, gait and impaired ability to respond to external perturbations [77].
   (e) Alzheimer's disease (AD) patients exhibit an altered gait pattern and increased gait stability. The prevalence of falls in these patients is higher to that of their healthy age-matched counterparts [3].
2. Cardiovascular problems
   (a) Orthostatic Hypotension (OH) is "a sustained reduction of systolic blood pressure of at least 20 mmHg or diastolic blood pressure of 10 mmHg

within 3 minutes of standing [78]." This condition affects approximately 30% of older adults living in the community and 70% of those living in nursing homes [79]. In a study including 722 patients with uncontrolled hypertension, older adults with OH had a higher fall risk than those without OH [80].

(b) Atrial Fibrillation (AF). A study involving 442 patients identified AF as an independent risk factor for nonaccidental falls in elderly patients admitted to the emergency room with a fall complaint [81]. In this sample of older adults, the prevalence of AF was significantly higher in those with a non-accidental fall than in patients with an accidental fall.

3. Visual problems

   (a) Cataracts, an abnormal increase in the opacity of eye lenses, are a common cause of impaired vision in older people, affecting approximately 16% of those over the age of 65 [72]. A study of 3,299 people over the age of 45 years reported that cataracts were significantly associated with a history of multiple falls in the previous 12 months [77].

   (b) Glaucoma, a term comprising a group of diseases characterised by an increase in intraocular pressure, produces alterations in the visual field. Glaucoma affects approximately 3% of people over the age of 65 and has been reported to be associated with increased fall risk in retrospective and prospective studies [72].

4. Osteoarthritis is a degenerative disease of articular cartilage that mainly affects the major joints of the lower limb, leading to structural deformity and decreased range of motion [77]. Older people with knee and hip osteoarthritis have difficulty performing the activities of daily life. Several studies have found osteoarthritis to be an independent risk factor for falling [77].

5. Urinary incontinence is a common problem in older adults, with up to 34% of older men and 55% of older women suffering from it [77]. Both retrospective and prospective studies have consistently reported urinary incontinence to be a strong risk factor for falls in community-dwelling and institutionalised older people [77].

6. Cognitive and mental factors

   (a) Dementia affects between 6 to 10% of community-dwelling older people and has been reported as a strong risk factor for falls in several studies

[77]. The mechanisms underlying this relationship are unknown as yet. However, it has been suggested that the cognitive impairment associated with dementia limits the person's ability to deal with environmental hazards, increasing the risk of falling [77].

(b) Depression is a common mental health condition in later life, with 15% of community-dwelling older adults reporting significant depressive symptoms, while in nursing homes the prevalence can be as high as 25% [77]. Older adults suffering from depression have a 7.5 times higher likelihood of experiencing a fall than their healthy counterparts [77]. The mechanisms underlying the relationship between depressive symptoms and falls are not yet fully understood. However, it has been suggested that older people who suffer are less physically active, which increases their fall risk due to reduced muscle strength and coordination [76].

Medication. The use of multiple medications is significantly associated with an increased fall risk [82]. Initially, multiple drug use was understood to be a proxy measure for poor health. However, there is increasing evidence suggesting that falls linked to use of medication are the result of adverse reactions to one or more drugs, harmful drug interactions and incorrect use [82].

Besides, some studies have investigated the associations between an increased fall risk in older adults and the use of specific drug groups [3, 82]. Among these drug groups, psychoactive medications (including antidepressants, sedatives/hypnotics, antipsychotics, and drugs used to treat bipolar disorder and dementia), as well as cardiovascular medications (including anti-arrhythmics and cardiotonics) are weakly but significantly associated with fall risk.

Sleep. Healthy ageing is accompanied by a reduced ability to initiate and maintain sleep, resulting in sleep discontinuities (i.e. sleep fragmentation) and shorter sleep duration [83]. Some prospective studies have found associations between sleep and risk of falling in older adults [16–19].

A study of 2,978 community-dwelling older women found that the odds of having 2 or more falls in the subsequent year was higher for women who slept 5 hours or less per night than for those who slept 7–8 hours per night [17]. Indexes of sleep fragmentation (i.e. "interrupted" sleep) were also associated with an increased risk of falls. For instance, women with poor sleep efficiency (less than 70% of the time in bed spent sleeping) had a 1.36-fold increased odds of falling compared with the others [17].

Similarly, a study of 3,101 community-dwelling older men found that the odds of having 2 or more falls in the subsequent year was higher for men who slept 5 hours or less per night than for those who slept 7–8 hours per night [18]. Low sleep efficiency (less than 70%) was also associated with a higher fall risk.

The association between sleep duration and fall risk was confirmed in a systematic review and meta-analysis of seven observational studies [84]. The meta-analysis showed that the odds of having one or more falls in the past or subsequent year was higher for older adults who had shorter sleep durations than for those who had "normal" sleep durations.

Additionally, a recent study of 1,071 community-dwelling older adults investigated the association between subjective sleep quality and risk of falls in older people [19]. Multivariable analysis revealed that participants reporting worse subjective sleep quality had significantly higher odds of experiencing falls during the 1-year follow-up period. This association was similarly significant in subgroup analyses for older men and women.

The findings above are relevant for fall risk assessment and prevention in older adults. Still, to the best of the author's knowledge, sleep has not yet been included in any fall risk assessment programme.

2.3.3.2 Extrinsic risk factors

Identifiable environmental hazards are not significant risk factors for falling among older people as a whole. This is particularly the case for older people's own homes [85]. However, the interaction between an older person's physical disabilities and exposure to environmental stressors does appear to be central in their risk of falling. Although falling rates are lower in healthy older people than their frailer counterparts, environmental hazards have a higher contribution to falls in this group.

The *home environment* plays an essential role within this category of risks for falls. For example, poor lighting, slippery floor surfaces and loose rugs may increase the risk of falls. These factors are more problematic in individuals with visual impairment [3]. Contrast sensitivity diminishes in older age and may be further compromised by concurrent ocular disease.

Footwear is another essential extrinsic risk factor, which affects postural stability and thus influences the incidence of accidental falls [3]. In a systematic review, Menant *et al.* reported that older people who wore slippers had a higher falls risk score than those who walked barefoot or with fastened shoes [86].

2.4 Assessment of balance control

Multiple methods to assess balance in older adults have been suggested, ranging from simple questionnaires and functional mobility tests requiring no more than a stopwatch, to complex techniques relying on force-sensing platforms and optical motion capture systems, among other items of equipment [4, 8]. These methods are often used to identify balance impairments and their cause, to assess fall risk and to assess the effects of interventions meant to improve balance control. The most common clinical tests assess balance in unperturbed standing (static balance) or balance in gait or other functional tasks (dynamic balance). In general, these clinical tests quantify the ability to maintain balance during a particular task or the quality of the performance of a balance task. Also, there are physiological tests that assess the functioning of specific subsystems involved in balance in order to identify potential causes for impaired balance [4]. This section presents the techniques and methods to assess balance that are relevant to this research.

2.4.1 Subjective assessment of balance problems

Questionnaires are the simplest tool to assess fall risk in older adults. These tools often explore indicators of prospective falls, such as the individual's fear of falling or balance confidence [87]. Fear of falling is defined as the concern that one may fall while performing daily-life activities. High fear of falling is associated with worse balance performance in standing and gait [2]. It can be measured with the Falls Efficacy Scale International (FES-I), a 16-item questionnaire [88], or its shortened 7-item version [89].

A history of falls in the previous year is also a strong predictor of future falls, thus an important indicator of impaired balance [56]. Hence, clinical fall risk assessment often starts with the clinician asking the person about her fall history.

Another subjective tool for the assessment of balance impairments is the Mini-Balance Evaluation Systems Test (Mini-BESTest). This test contains 14 items in four different domains: anticipatory postural adjustment, reactive postural response, sensorial organisation and gait stability. Each item is scored from 0 (abnormal performance) to 2 (normal performance) points, producing a maximum total score of 28 points [90].

2.4.2 Static balance tests

Static balance tests can be performed by measuring postural sway in unperturbed standing with a motion capture system, comprising body markers that are placed

on important body landmarks and infrared cameras that capture the movement of these markers. Alternatively, wearable inertial sensors can be used to measure the movement of body segments. In any case, data collected with the cameras or the inertial sensors are used to estimate the location of the body CoM over time or CoM excursions. This technique, known as *static posturography*, allows measuring the amplitude, velocity, and acceleration of movements of the body CoM in Anterior-Posterior (AP) and Medial-Lateral (ML) directions [25].

Most frequently, static balance is assessed by measuring Centre of Pressure (CoP) motion in unperturbed standing. The CoP is the point of application of the vertical ground reaction force vector and represents a weighted average of all the pressures over the surface of the area in contact with the ground [1]. It is typically acquired with a force-sensing platform, which produces a two-dimensional time-series representing the CoP trajectories in the AP and ML axes. In other words, the CoP is a bivariate distribution, jointly defined by its AP and ML coordinates [91].

To assess the balance control system in a natural state, subjects are usually allowed to stand still in a comfortable, self-selected stance, facing towards the positive AP direction of the force platform [91]. In bidepal standing, the net CoP lies somewhere between the two feet, depending on the load taken by each lower limb. Yet, there are separate CoPs for each foot. If one force platform is used then, only the net CoP is available. Two force platforms are required to quantify the CoP changes within each foot [1].

The body CoM and CoP are independent, yet there is an interplay between them. Figure 2.4 illustrates the difference between CoP and CoM. Briefly, the location of the CoP under the feet is a direct reflection of the neural control of the ankle and hip muscles in order to maintain the CoM over the BoS, as described in subsection 2.2.1.

Several manipulations can be introduced during static posturography in order to assess balance control under different testing conditions. Popular manipulations are decreasing visual feedback (e.g. eye closure), decreasing proprioceptive feedback (e.g. standing on a compliant surface) or a combination thereof [25]. Figure 2.5 shows the CoP excursions from a young adult and an older adult during unperturbed standing under four different surface-vision testing conditions: eyes open-rigid surface, eyes closed-rigid surface, eyes open-foam surface and eyes closed-foam surface.

Analysis of centre of pressure data. Filtering of the signal is usually the first step in CoP analysis [26]. For the study of unperturbed standing, a fourth-order

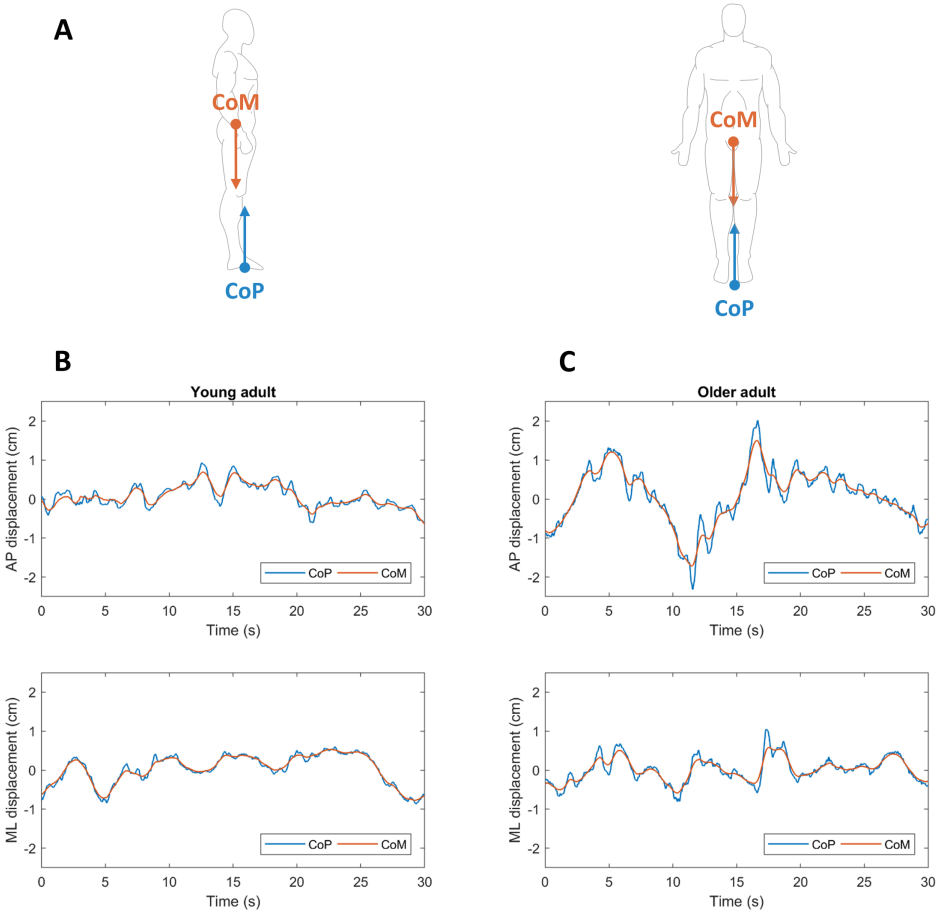

Figure 2.4: Illustration depicting the difference between centre of pressure (CoP) and centre of mass (CoM) displacements in the anterior-posterior (AP) and medial-lateral (ML) directions during the quiet standing posture **(A)** and examples of the CoP and CoM for a young adult (25 years old) **(B)** and an older adult (70 years old) **(C)**. Data sourced from a public dataset [27].

Butterworth low-pass filter with a cut-off frequency of 5–10 Hz has been suggested, as the components of the CoP signal frequency are below 10 Hz (with most of them below 5 Hz) [26, 91].

Subsequently, it is a common procedure to remove the mean of the CoP time-series [26, 91]. The rationale for such a procedure is that the mean position of the CoP is not of interest, as it is simply dependent on the absolute position of the subject on the force plate, which is not necessarily controlled. In mathematical terms, given two time-series of length N, AP_O and ML_O, which represent the CoP displacement relative to the origin of the force plate coordinate system, the mean

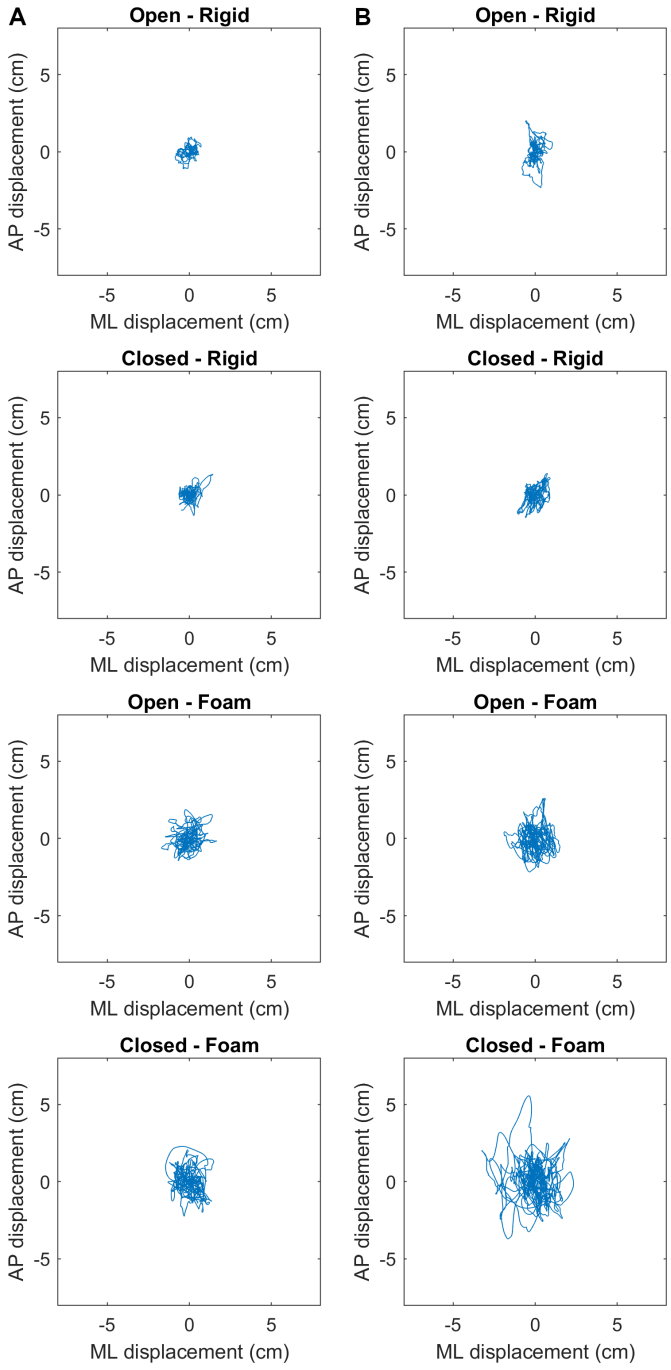

Figure 2.5: Centre of pressure excursions during quiet standing for **(A)** a young adult (25 years old) and **(B)** an older adult (70 years old) under four different vision-surface testing conditions: open-rigid, closed-rigid, open-foam and closed-foam. Data sourced from a public dataset [27].

position of the CoP is defined by the arithmetic mean of AP_O and ML_O, given by [91]:

$$\overline{AP} = \frac{1}{N}\sum_{n=1}^{N} AP_O(n) \tag{2.1}$$

$$\overline{ML} = \frac{1}{N}\sum_{n=1}^{N} ML_O(n) \tag{2.2}$$

The AP and ML coordinates of the CoP relative to its mean position are computed from equations 2.1 and 2.2 as follows [91]:

$$AP(n) = AP_O(n) - \overline{AP} \qquad \text{for } n = 1, \ldots, N \tag{2.3}$$

$$ML(n) = ML_O(n) - \overline{ML} \qquad \text{for } n = 1, \ldots, N \tag{2.4}$$

Finally, the time-series AP and ML are characterised using a number of quantitative descriptors or measures [91]. These measures can be categorised into global and structural [8, 26].

Global measures

The starting point of the analysis of CoP time-series is the calculation of their basic characteristics in the time and frequency domain. This approach assumes that the balance control system has a linear nature and thus can be characterised by measures computed over the entire time-series, hence the name *global measures* [8, 26]. Time-domain global measures include amplitude and standard deviation, while frequency-domain measures include mean and median frequency of the signal.

The global CoP measures used in later chapters are:

1. *Amplitude of displacement (AdCP)* is the distance between the maximum and minimum CoP displacement for each direction [8, 26]:

$$AdCP_{AP} = \max(AP) - \min(AP) \tag{2.5}$$

$$AdCP_{ML} = \max(ML) - \min(ML) \tag{2.6}$$

2. *Standard deviation (SD)* represents the dispersion of the CoP displacement around the mean for each direction. Since the time-series AP and ML have a

mean equal to zero, their standard deviation can be computed by [8, 26, 91]:

$$SD_{AP} = \sqrt{\frac{1}{N-1}\sum_{n=1}^{N} AP(n)^2} \tag{2.7}$$

$$SD_{ML} = \sqrt{\frac{1}{N-1}\sum_{n=1}^{N} ML(n)^2} \tag{2.8}$$

3. *Mean velocity (MV)* is the average velocity of the CoP in the AP and ML directions and is approximated by dividing the total length of the CoP excursion in each direction by the duration of the recording, T [91]:

$$MV_{AP} = \frac{1}{T}\sum_{n=1}^{N-1} |AP(n+1) - AP(n)| \tag{2.9}$$

$$MV_{ML} = \frac{1}{T}\sum_{n=1}^{N-1} |ML(n+1) - ML(n)| \tag{2.10}$$

4. *Total length (DOT)* quantifies the magnitude of the two-dimensional displacement of the CoP over the BoS, and is approximated by the sum of the distances between consecutive points of the CoP excursion [91]:

$$DOT = \sum_{n=1}^{N-1} \sqrt{[AP(n+1) - AP(n)]^2 + [ML(n+1) - ML(n)]^2} \tag{2.11}$$

5. *Total mean velocity (TMV)* is the average velocity of the CoP in the AP and ML directions and is approximated by dividing the total length of the CoP excursion by the duration of the recording, T [91]:

$$TMV = \frac{DOT}{T} \tag{2.12}$$

6. *Area* is an estimate of the dispersion of the CoP data in the AP and ML, obtained through the computation of the area of the ellipse that contains 95% of the CoP data points [8, 26]. The most common method to calculate this area is through the statistical method of analysis of the principal components suggested by Duarte *et al.* [26]:

$$Area = \pi \times prod(2.4478 \times \sqrt{svd(val)}) \tag{2.13}$$

where *val* is a 2–by–2 matrix containing the eigenvectors of the 2–by–2 matrix obtained from the calculation of the covariance between time-series AP and ML, *svd* is an operator that returns the singular values of matrix *val*, and *prod* is the product of the elements in the matrix [26].

The existence of age-related differences in CoP global measures has been widely acknowledged by researchers and clinicians [8, 26, 91]. Yet, their predictive value for fall risk is not clear as yet [92]. Therefore, the interpretation of global measures is still open to discussion.

A limitation of global measures is that they are not sensitive to structural variations in CoP excursions, a feature which could potentially provide more insights into the mechanisms of balance control. A complementary approach is the use of measures that are sensitive to structural variation in time-series, i.e. structural measures.

Structural measures

Nonlinear dynamic time-series analysis has been proposed as a tool to investigate the characteristics and mechanisms of physiological systems and, in particular, of the balance control system [8, 26, 29]. The assumption underlying this approach is the idea that the balance control system must be considered a nonlinear system (i.e. its reactions are not proportional to the applied stimuli) [20]. In contrast to global measures, quantitative descriptors of nonlinear dynamics are sensitive to structural variations within time-series, hence they are often referred to as *structural measures* within the balance research community [8, 26].

Unfortunately, the estimation of nonlinear quantitative descriptors or measures usually requires very long time-series [29]. In practice, the data obtained experimentally are often short in length. Static posturography, in particular, generally produces CoP time-series of short duration (i.e. 20-60 seconds), especially when assessing older adults as it can be challenging for some of them to stand still for one or more minutes [26, 188]. Therefore, nonlinear CoP time-series analysis needs the application of nonlinear measures that can be estimated robustly using short data.

Approximate Entropy (ApEn) [110] and Sample Entropy (SampEn) [111] are nonlinear measures well suited to the analysis of short and noisy data. Thus, they are extensively used in later chapters for the analysis of CoP time-series. These methods quantify the regularity or self-similarity of time-series by examining them for similar epochs or subseries: more frequent, similar subseries lead to lower entropy values. Thus low ApEn and SampEn values reflect a high degree of regularity or self-similarity [110, 111]. Regarding CoP time-series analysis, relatively high entropy

values may be indicative of balance control mechanisms that are too random to command balance properly, whereas relatively low values may describe a balance control that is too stiff to cope with situations that require flexibility [21].

The paragraphs below present the mathematical formulation and interpretation of ApEn and SampEn, as well as a comparison between both algorithms.

Approximate Entropy (ApEn). Given the original time-series $\langle u(n) \rangle$ with the form

$$\langle u(n) \rangle = u(1), u(2), \ldots, u(N)$$

where N is the total number of data points (i.e. data length), ApEn is defined and computed by the following step-by-step algorithm [28, 110]:

1. Fix m, an integer, and r, a positive real number. m represents the length of the epochs or subseries to be compared to each other, and r specifies the similarity tolerance for accepting matches between subseries.

2. Form a sequence of subseries $X(1), X(2), \ldots, X(N-m+1)$ such that:

$$X(i) = [u(i), \ldots, u(i+m-1)] \qquad \text{for } i = 1, \ldots, N-m+1 \tag{2.14}$$

3. For a given $X(i)$, find:

$$N_r^m(i) = \text{number of } d[X(i), X(j)] \leq \pm r \times SD_u \qquad \forall j \tag{2.15}$$

where $d[X(i), X(j)]$ is the distance between $X(i)$ and $X(j)$, defined as:

$$d[X(i), X(j)] = \max\left[|x(i+k) - x(j+k)|\right] \qquad \text{for } k = 0, \ldots, m-1 \tag{2.16}$$

and SD_u is the standard deviation of the original time-series $\langle u(n) \rangle$, i.e.,

$$SD_u = \sqrt{\frac{1}{N-1} \sum_{n=1}^{N} \left[x(n) - \frac{1}{N} \sum_{n=1}^{N} x(n) \right]^2} \tag{2.17}$$

Then, compute:

$$C_r^m(i) = \frac{N_r^m(i)}{N-m+1} \tag{2.18}$$

This step is performed over all i, i.e. $i = 1, \ldots, N-m+1$.

4. Calculate

$$\phi_r^m = \frac{1}{N-m+1} \sum_{i=1}^{N-m+1} \ln C_r^m(i) \tag{2.19}$$

5. Increase the subseries length to $m+1$ and repeat steps 2 to 4 to find ϕ_r^{m+1}

6. Estimate ApEn by computing

$$ApEn(m, r, N) = \phi_r^m - \phi_r^{m+1} \tag{2.20}$$

The meaning of ApEn can be intuitively explained with the aid of Figure 2.6, which shows a time-series with 30 points (this example has been adapted from literature [28]). For $m = 2$, each $X(i) = [x(i), x(i+1)]$ is a line segment joining every two consecutive data points [e.g., when $i = 8$, $X(8) = [x(8), x(9)]$ is shown as a thick line in Figure 2.6(A)]. Two horizontal bands I and II, each of width $2 \times r \times SD_u$, can be drawn around $x(i)$ and $x(i+1)$. They are the tolerance regions that satisfy the requirement $d[X(i), X(j)] \leq 2 \times r \times SD_u$. As shown in Figure 2.6(A), in addition to $X(8)$ itself, there are three other vectors satisfying the requirement; namely $X(15)$, $X(19)$ and $X(24)$. Thus $N_r^{m=2}(i = 8) = 4$ and $C_r^{m=2}(i = 8) = 4/(N - m + 1) = 4/29 = 0.1379$. In other words, $N_r^{m=2}(i)$ is the total number of line segments (i.e. two-point subseries) formed by all the consecutive points in the sequence that are "close" to $X(i)$ within the tolerance $\pm r \times SD_u$ and $C_r^{m=2}(i)$ is the frequency of its occurrence. Thus, ϕ_r^m represents the average frequency of all m-point patterns in the sequence being close to each other.

Similarly, when $m = 3$, $X(i) = [x(i), x(i+1), x(i+2)]$ is a three-point pattern formed by joining every three consecutive data points (for instance, $X(8) = [x(8), x(9), x(10)]$ is shown in Figure 2.6(B)) and $N_r^{m=3}(i)$ is the total number of such three-point patterns $X(j) = [x(j), x(j+1), x(j+2)]$ in the time-series that are close to $X(j)$ within the tolerance $\pm r \times SD_u$. As shown in Figure 2.6(B), for the given example, only $X(15)$ and $X(19)$ satisfy the requirement, but $X(24)$ fails because its third element, $x(26)$, falls outside the tolerance band III of $x(10)$. In this case, $C_r^{m=3}(i)$ is the frequency of occurrence of three-point patterns in the sequence that are close (within the tolerance band) to the three-point pattern $X(i) = [x(i), x(i+1), x(i+2)]$. Thus, ϕ_r^m represents the average frequency of all $m+1$-point patterns in the sequence being close to each other.

Finally, $ApEn(m, r) = \phi_r^m - \phi_r^{m+1}$ is the difference between the frequency that all the two-point patterns in the sequence are close to each other and the frequency that all the three-point patterns in the sequence are close to each other.

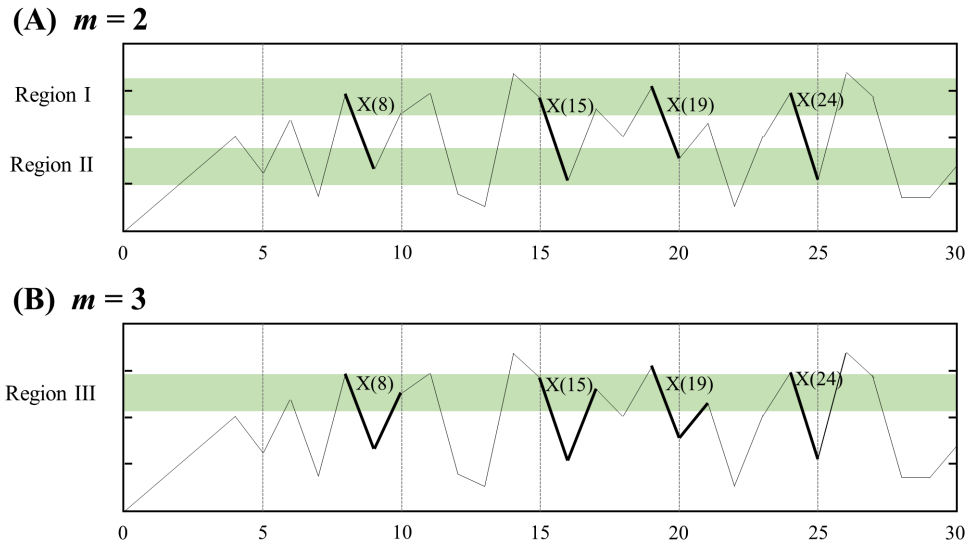

Figure 2.6: Graphical interpretation of approximate entropy. Adapted from the literature [28].

Thus, $ApEn(m = 2, r)$ expresses the degree of new pattern generation when the dimension m decreases from 3 to 2. A large value of ApEn means that the chance of new pattern generation is high, so the time-series is irregular (e.g. white noise); conversely, a small value of ApEn corresponds to a regular time-series (e.g. a periodic signal) [110].

Sample Entropy (SampEn). Given the original time-series $\langle u(n) \rangle$ with the form

$$\langle u(n) \rangle = u(1), u(2), \ldots, u(N)$$

where N is the total number of data points (i.e. data length), SampEn is defined and computed by the following step-by-step algorithm [111]:

1. Fix m, an integer, and r, a positive real number. m represents the length of the epochs or subseries to be compared to each other, and r specifies the similarity tolerance for accepting matches between subseries.

2. Form a sequence of subseries $X(1), X(2), \ldots, X(N - m + 1)$ such that:

$$X(i) = [u(i), \ldots, u(i + m - 1)] \qquad \text{for } i = 1, \ldots, N - m + 1$$

3. For a given $X(i)$, find:

$$N_r^m(i) = \text{number of } d[X(i), X(j)] \leq \pm r \times SD_u \qquad \forall j \neq i \tag{2.21}$$

where $d[X(i), X(j)]$ is the distance between $X(i)$ and $X(j)$, defined as:

$$d[X(i), X(j)] = \max\left[|x(i+k) - x(j+k)|\right] \qquad \text{for } k = 0, \ldots, m-1 \tag{2.22}$$

and SD_u is the standard deviation of the original time-series (equation 2.17).

Then compute

$$B_r^m(i) = \frac{N_r^m(i)}{N - m - 1} \tag{2.23}$$

This step is performed over all i; i.e. $i = 1, \ldots, N - m$.

4. Calculate

$$B_r^m = \frac{1}{N-m} \sum_{i=1}^{N-m} B_r^m(i) \tag{2.24}$$

5. Increase the subseries length to $m + 1$ and repeat steps 2 to 3 to find $A_r^m(i)$ for $i = 1, \ldots, N - m$ and then compute

$$A_r^m = \frac{1}{N-m} \sum_{i=1}^{N-m} A_r^m(i) \tag{2.25}$$

6. Estimate of SampEn by computing

$$SampEn(m, r, N) = -\ln \frac{A_r^m}{B_r^m} \tag{2.26}$$

In the above definition, B_r^m is the probability that two subseries will match for m points, whereas A_r^m is the probability that two subseries will match for $m+1$ points [111]. As a result, SampEn is the negative natural logarithm of the conditional probability that two subseries within a tolerance $r \times SD_u$ for m points remain within $r \times SD_u$ of each other at the next point [111]. Therefore, a lower SampEn value also indicates more self-similarity or regularity in the time series.

Comparison between ApEn and SampEn

As mentioned above, both ApEn and SampEn quantify the regularity of time-series, with lower entropy values reflecting a higher degree of regularity. However, a seemingly minor difference in the criterion used by each algorithm to establish similarity

between subseries leads to a substantial difference between them: ApEn counts self-matches when comparing subseries $X(i)$ and $X(j)$, whereas SampEn does not. This difference is made explicit by comparing equations 2.15 and 2.21. In practical terms, the fact that ApEn counts self-matches inherently produces a bias towards regularity (i.e. an inflated entropy value).

It has also been mentioned that ApEn and SampEn can be estimated on short and noisy data. The first feature is related to the fact that both measures are based on conditional probabilities, which require less data than joint probabilities to produce a reliable estimate [28]. Nevertheless, SampEn shows a more consistent behaviour than ApEn over a wider range of data lengths [111]. The second feature is the result of allowing a tolerance range, given by $\pm r \times SD_u$ (equations 2.15 and 2.21), to establish similarity between subseries in order to account for the presence of noise in the data [110, 111].

Research gaps

The appropriate selection of parameters m (subseries length), r (similarity tolerance) and N (data length) is critical. Traditionally, for clinical data, m is to be set at 2 or 3, r is to be set between 0.1 and 0.25 times the standard deviation of the data and N as equal to or greater than 1000 [110, 111]. However, these recommendations were based on the analysis of cardiac and respiratory time-series, thus do not always produce optimal results for all types of data. Therefore, an investigation of the effects of changing parameter values on the computation of ApEn and SampEn for specific types of data is needed. A previous study addressed this issue in the context of spatiotemporal gait measures analysis (i.e. step length, step width and step time) [112]. However, the issue has not been investigated systematically when dealing with CoP time-series.

Moreover, the existence of group and testing-condition differences in ApEn and SampEn values has been proved in previous studies. However, the predictive value of ApEn and SampEn for fall risk has not yet been formally investigated.

2.4.3 Dynamic balance tests

Dynamic posturography assesses the response to experimentally-induced balance perturbations. A first approach is to use a movable support surface (e.g. a movable force-sensing platform). Movable platforms can produce rapid and brief horizontal and vertical translations, rotations and a combination thereof. Their use allows measuring the subject's ability to maintain or regain balance after perturbations. An alternative approach is to apply external perturbations aimed directly at upper

body segments, for example by pushing or pulling the trunk, shoulder or pelvis [25].

Since dynamic posturography was not used during this research, a detailed description of the methods used to quantify dynamic balance is beyond the scope of this thesis. Further information on this topic can be found in literature [25].

2.4.4 Functional balance tests

Functional balance tests measure the ability to maintain balance in tasks such as getting up from a chair, standing, and walking. The Tinetti Balance Test or Performance-Oriented Mobility Assessment (POMA) [113], the Berg Balance Scale (BBS) [114, 115] and the Timed-Up-and-Go test (TUG test) [116, 117] are among the most popular functional balance tests since they are inexpensive and straightforward. The outcomes of these functional balance tests are often interpreted in relation to fall risk. For instance, the TUG test is often used to assess fall risk but does not differentiate older fallers from non-fallers [118]. Also for the other tests, there is no or minimal evidence for a predictive value concerning fall risk [119].

Currently, instrumented versions of functional balance tests are developed and used with the aim of obtaining objective and precise results and achieving a higher sensitivity to subtle balance impairments [12]. Wearable inertial sensors (e.g. micro-electronic devices integrating accelerometers and gyroscopes) are among the most used sensors since they provide kinematic data of movements in a functional task such as walking and getting up from a chair (Figure 2.7) [10]. However, some reviews on the topic have acknowledged an issue in the variety of sensor placements, functional tasks and measured variables that have been used in previous studies [11, 12]. This heterogeneity hinders a consensus on the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults.

2.5 Sleep in older adults

2.5.1 Normal sleep and sleep structure

Sleep is a reversible behavioural state of perceptual disengagement from and unresponsiveness to the environment, accompanied by alternating cycles of physiological processes [120].

Sleep is classified into Non-Rapid Eye Movement (NREM) and Rapid Eye Movement (REM) sleep, with NREM further divided into stages N1 to N3. NREM and REM sleep occur in alternating cycles, each lasting approximately 90 to 110 minutes in healthy adults, with approximately 4 to 6 cycles during an average 6 to

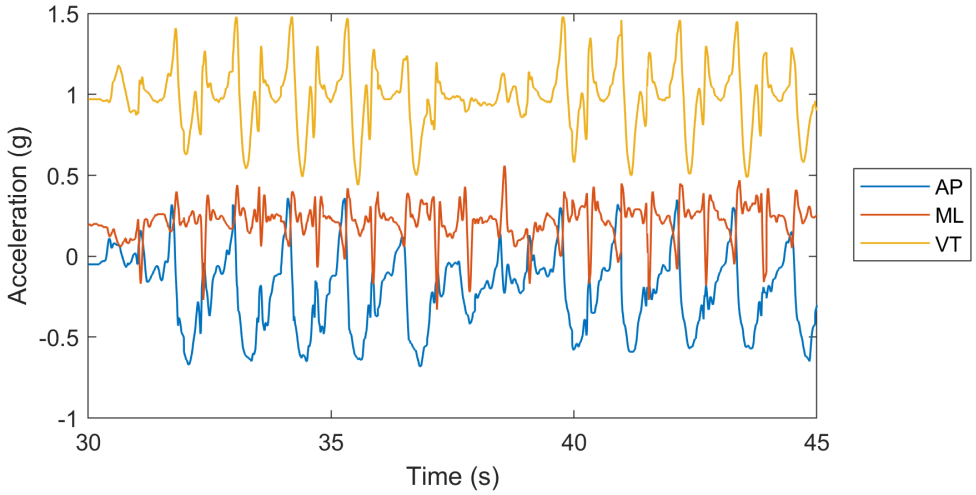

Figure 2.7: Acceleration signals from a lower leg during gait. These signals were recorded with the accelerometer embedded in a smartphone (Samsung Galaxy Core Prime) while the subject walked 3-metre long straight course, turned 180 degrees and walked back. The cyclical nature of gait is apparent from the anterior-posterior and vertical acceleration signals. AP anterior-posterior axis, ML medial-lateral axis, VT vertical axis. Data collected by the author.

8 hour sleep period [121]. However, these timings are dependent on many factors, such as age, use of medication, and physical and mental health.

In healthy young adults, NREM sleep accounts for 75 to 90% of sleep time, while REM sleep accounts for 10 to 25% of sleep time. NREM sleep comprises 3 to 5% in stage N1, 50 to 60% in stage N2 and 10 to 20% in stage N3. Stages N1 and N2 are known as light sleep and stage N3 as deep sleep or Slow Wave Sleep (SWS). Cardiovascular activity is at a 24-h low in deep sleep, whereas there is little difference between REM sleep and wakefulness.

Sleep stages are often interrupted by micro-arousals (1.5 to 3 seconds of increased physiological activity) and short awakenings (shorter than 15 seconds).

2.5.2 Sleep parameters

Some parameters concerning the quantity and quality of sleep are usually included in a sleep study report [122]:

1. Sleep Onset Latency (SOL), or sleep latency, is defined as the duration of time between the moment a person attempts to sleep until he/she falls asleep. SOL reflects the person's ability to initiate sleep.

2. Wake After Sleep Onset (WASO) is defined as the cumulative duration of all

Table 2.2: Summary of sleep parameters usually reported in a sleep study [122]

Parameter	Units	Definition	Interpretation
SOL	minutes	Duration of time between the moment a person attempts to sleep until he/she falls asleep	Ability to initiate sleep
WASO	minutes	Cumulative duration of all periods of wakefulness occurring after sleep onset	Ability to maintain sleep. A more interrupted or fragmented sleep is deemed of poor quality
TST	hours	Total amount of sleep time, from sleep onset to sleep offset, but excluding WASO	Sleep duration or quantity
SE	%	Percentage of total time in bed spent in sleep	A proxy measure of sleep quantity and quality

SOL sleep onset latency, *WASO* wake after sleep onset, *TST* total sleep time, *SE* sleep efficiency

periods of wakefulness occurring after sleep onset. WASO is a measure of sleep fragmentation and reflects the person's ability to maintain sleep.

3. Total Sleep Time (TST) is the total amount of sleep time, from sleep onset to sleep offset, but excluding WASO.

4. Sleep Efficiency (SE) refers to the percentage of total time in bed spent in sleep. It is a combined reflection of the ability to initiate and maintain sleep.

2.5.3 Age-related changes in sleep

Healthy ageing is accompanied by a reduced ability to initiate and maintain sleep. Some of the changes in sleep architecture that are observed from the fifth decade and beyond are [83]:

1. earlier bedtimes and rise times

2. longer sleep latency (i.e.SOL)

3. shorter sleep duration (i.e. TST)

4. increased sleep fragmentation (i.e. less consolidated sleep with more awakenings, arousals, or transitions to lighter sleep stages)

5. more fragile sleep (i.e. higher likelihood of being woken by external sensory stimuli)
6. reduced amount of deeper sleep
7. increased time spent in lighter NREM stages 1 and 2
8. shorter and fewer NREM-REM sleep cycles
9. increased time spent awake throughout the night

Furthermore, sleep disorders are especially prominent in later life [83].

2.5.4 Assessment of sleep

2.5.4.1 Subjective assessment of sleep

The Pittsburgh Sleep Quality Index (PSQI) is a self-reported 19-item questionnaire that assesses sleep quality over the past 1-month time interval [30]. This instrument measures several aspects of sleep, producing seven component scores and one composite score. The component scores consist of subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. Each item is weighted on a 0 to 3 interval scale. The global PSQI score is then calculated by totalling the seven component scores, providing an overall score ranging from 0 to 21, where lower scores denote a healthier sleep quality. A global PSQI greater than five is interpreted as indicative of poor sleep [30].

A sleep diary provides the means to record daily sleep habits and disturbances over several days (e.g. bed and wake-up times, number and length of awakenings during the night). A standardised sleep diary, called the Consensus Sleep Diary (CSD), has been proposed by collecting, analysing and compiling sleep diaries from 25 sleep experts [31]. The information reported by the user in the sleep diary allows to estimate traditional sleep parameters (e.g. SOL, WASO and TST), as well as a score for subjective sleep quality, for each night.

The Epworth sleepiness scale (ESS) is a questionnaire designed to measure daytime sleepiness [123]. The responder is asked to score his or her propensity to fall asleep in eight situations involving different levels of stimulation (e.g. sitting and reading, watching TV and sitting and talking to someone). Significant differences in ESS scores have been observed between controls and patients suffering from sleep disorders characterised by excessive daytime sleepiness (e.g. narcolepsy and hypersomnia) [123]. However, ESS scores have been found to be uncorrelated with all

sleep parameters but one (namely, SOL) [123]. Therefore, this scale was discarded for the studies herein, since they focussed on sleep quantity and quality at night, not on daytime sleepiness.

2.5.4.2 Objective assessment of sleep

Polysomnography. *Polysomnography (PSG)* is the "gold standard" modality for sleep studies. As a minimum, it incorporates Electroencephalogram (EEG), Electrooculogram (EOG) and submentalis Electromyogram (EMG) recordings. These signals are then used to label 30-sec epochs into sleep stages (NREM stages N1 to N3 and REM) from which all other sleep parameters are calculated [33, 34]. Other physiological variables can be collected if needed (e.g., respiration, heart rate, tibialis muscle movement, oximetry).

Sleeping naturally while wearing a large number of sensors and wires is virtually impossible. Moreover, PSG studies are expensive and require specialised facilities and staff to score the data. There are many home sleep recording systems on the market which aim to reduce the financial cost per patient and reach a larger population. However, the patient has to place the sensors in the correct positions without the guidance of a specialist, which often leads to poor-quality data [121].

Actigraphy. Actigraphs are electronic devices that can measure and store limb or body accelerations over periods lasting from a few hours to days or even weeks. The data collected are displayed on a computer and analysed in wake-sleep based on activity levels for individual epochs. Actigraphy is thus based on the fact that during sleep little or no movement occurs, whereas during wake an increase in movement frequency and amplitude is observed. Actigraphy is much less expensive and unobtrusive than PSG [32].

Modern actigraphs are the size of a wristwatch and collect digitised data. Physical movement is generally sampled several times per second and stored in 1-minute epochs. The three primary ways in which signals can be digitised are the threshold or Zero Crossing Mode (ZCM), Time Above Threshold (TAT) mode and Proportional Integrating Mode (PIM) [124].

In the ZCM, the signal voltage from the accelerometer is compared with the reference voltage, and each zero crossing generates an activity count; each movement above the reference signal generates 2 zero crossings since the signal eventually recedes below the threshold. The frequency of zero crossings is measured for every epoch.

In the TAT mode, the signal voltage is compared with the reference voltage

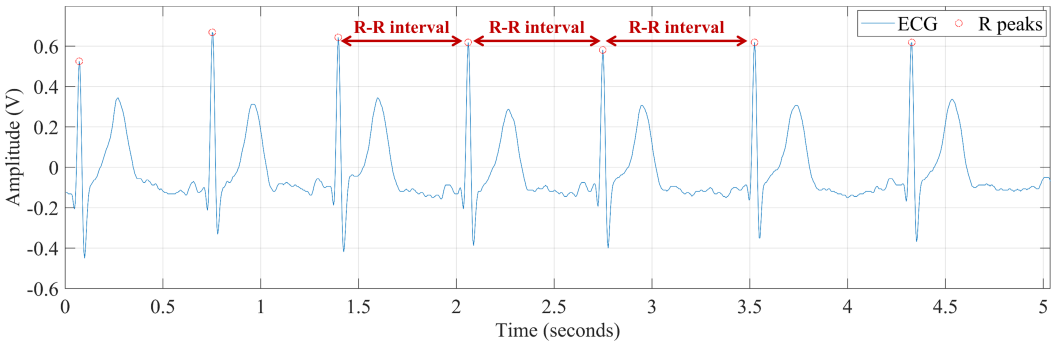

Figure 2.8: Electrocardiogram with highlighted R-R intervals. Data collected by the author.

and a count is generated and stored in memory every 10th of a second while the signal voltage remains above the threshold. The TAT mode is mostly used for daytime activity monitoring because it is thought to be indicative of the vigour of measured activity.

In the PIM, the area under the rectified analogue signal is measured for each epoch, and the accumulated count is stored. The PIM measures movement intensity by summing the deviations from 0 V every 10th second.

For clinical use, once the data are digitised, computer algorithms automatically score wake and sleep and provide the user with summary statistics. These computer algorithms generally supply information on sleep latency, sleep duration, sleep efficiency, wake after sleep onset time, number of awakenings and time between awakenings [32].

Heart rate variability analysis. Heart Rate Variability (HRV) analysis has been proposed as a tool to explore autonomic cardiac modulation during sleep [35]. HRV is the variation over time of the interval between consecutive heartbeats (or similarly in the instantaneous Heart Rate (HR)) due to autonomic neural regulation of the heart and the circulatory system (Figure 2.8).

HRV is controlled by the activity of the Autonomic Nervous System (ANS). The ANS connects the body's nervous system to the main physiological systems, regulating virtually all of the unconscious mechanisms of the human body, including the heart beat [125]. The ANS has two components: the sympathetic and the parasympathetic branches. Sympathetic stimulation causes an increase in HR by increasing the firing rate of pacemaker cells in the hearts sino-atrial node. Parasympathetic activity decreases the firing rate of pacemaker cells and the HR, providing a regulatory balance in physiological autonomic function. The individual regular con-

tributions from sympathetic and parasympathetic autonomic activity regulate the heartbeat intervals (R-R intervals) of the QRS complex in the Electrocardiogram (ECG) (Figure 2.9), at distinguishable frequencies. Sympathetic activity is related to the low-frequency range (0.04-0.15 Hz) while parasympathetic activity is related to the high-frequency range (0.15-0.4 Hz) of modulation frequencies of the HR. This difference in frequency ranges allows HRV analysis to separate sympathetic and parasympathetic contributions evident [126].

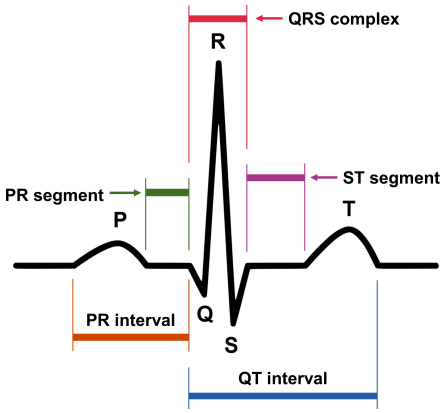

Figure 2.9: ECG waveform. Image marked as public domain.

HRV analysis is the ability to assess overall cardiac health and the state of ANS responsible for regulating cardiac activity [126].

HRV is a useful signal for understanding the status of the ANS. The balancing action of the sympathetic nervous system and parasympathetic nervous system branches of the ANS controls the HR. Increased sympathetic activity or diminished parasympathetic activity results in cardio-acceleration. Conversely, a low sympathetic activity or a high parasympathetic activity causes cardio-deceleration [126]. Therefore, the degree of variability in the HR provides information about the functioning of the nervous control on the HR.

A higher parasympathetic tone has been observed during NREM, particularly during deep sleep; in contrast, a higher sympathetic tone has been observed during wake intervals, REM and sleep arousals [35].

Variations in HR are characterised using several quantitative descriptors or measures, which are classified in three different categories: time-domain, frequency-domain analysis and nonlinear analysis [126]. A summary of the HRV measures used in this research is presented in Table 2.3. These measures were selected based on the relevance they have for sleep studies [35].

Time-domain measures are the simplest to calculate, thus require less compu-

tational power. Yet, they do not provide relevant information for sleep studies since they lack the ability to differentiate between sympathetic and para-sympathetic activity contributions to HRV. Therefore, they are not included in this thesis.

Frequency-domain measures are obtained from the spectral analysis of the sequence of NN intervals in the ECG recording. NN intervals are normal R-R intervals, thus excluding abnormal R-R intervals such as those produced by ectopic beats. Two main spectral components are distinguished in a spectrum calculated from ECG recordings in sleep studies: Low-Frequency (LF) and High-Frequency (HF) components. Measurement of LF and HF components is usually made in absolute values of power (ms^2), yet can also be measured in normalised units (n.u.). The details for the computation of these normalised measures can be found in Table 2.3. HF power describes the parasympathetic activity, whereas LF power describes both parasympathetic and sympathetic activity. Thus, the relationship between both branches usually is explored with the normalised frequency values and the LF/HF ratio. Broadly speaking, HRV analyses also include the Very Low-Frequency (VLF) component (i.e. $<$0.04 Hz) [127]. However, its association with autonomic activity is much less understood, especially in the context of sleep studies [35, 127]. Therefore, this component was not included in the studies herein. Wavelet-based methods for HRV analysis have been put forward as an alternative to overcome the limitations of conventional methods of spectral analysis based on the Fourier transform when dealing with non-stationary time-series [126]. Unfortunately, the relationship between sleep stages and wavelet-based features is not well understood as yet [35]. Alternatively, trend removal may be applied to the R-R interval time-series without affecting the components of interest for sleep studies (i.e. LF and HF) [127].

Nonlinear measures in HRV analyses are drawn from recent developments in the theory of nonlinear dynamics. It is generally accepted that these nonlinear techniques can improve the characterisation of biosignals. Two of these nonlinear measures that are of particular interest for HRV analysis in sleep studies are ApEn and SampEn, which have been described earlier. These entropy measures represent an index of complexity in the cardiac signal. An increase in complexity (i.e., an increase in the entropy measure) is associated with parasympathetic modulation, and its decrease is interpreted as the result of an increased sympathetic tone.

Table 2.3: Selected heart rate variability measures. HF power describes parasympathetic activity, whereas LF power describes both parasympathetic and sympathetic activity. The relationship between both branches is explored with the LF/HF ratio. Entropy measures represent an index of complexity in the cardiac signal. An increase in entropy is associated with parasympathetic modulation and a decrease with an increased sympathetic tone [126].

Frequency-domain measures		
LF	ms^2	Power in the low-frequency range (0.04–0.15 Hz)
LF norm	n.u.	LF power in normalised units LF norm = LF/(LF + HF) x 100
HF	ms^2	Power in the high-frequency range (0.15–0.4 Hz)
HF norm	n.u.	HF power in normalised LF norm = HF/(LF + HF) x 100
LF/HF		Ratio LF [ms^2] / HF [ms^2]
Nonlinear measures		
ApEn		A measure of the regularity in the NN time-series
SampEn		An improved measure of the regularity in the NN time-series

ApEn approximate entropy, *SampEn* sample entropy

2.6 Conclusions

This chapter has introduced balance control and falls in older adults (sections 2.2 and 2.3). Balance arises from the dynamic interaction of the sensory, motor and control systems. Impairment in any of these systems produces a deficit in balance control, which in turn increases the risk of falling. Falls are one of the most common and severe consequences of balance deficits in older age, with one in three adults over the age of 65 experiencing a fall each year.

Falls are associated with several risk factors, which are usually classified into two categories: intrinsic and extrinsic. Intrinsic risk factors comprise age-related changes to the balance control system (i.e. a decline in sensory and neuromotor control functions), some medical conditions and behavioural factors (e.g. multiple medications and short sleep duration). Extrinsic risk factors refer to environmental hazards, such as slippery surfaces and inadequate footwear.

Balance assessment is an essential component of fall prevention in older adults. This chapter has also introduced the methods and techniques for assessing balance control, emphasising those that are relevant to this thesis (section 2.4). Balance in standing is usually assessed via posturography; that is, the measurement of the body's CoP motion using a force-sensing platform or other instrumented surface (e.g. pressure-sensing insoles). Besides, balance in gait is usually performed

using an optical camera system. Furthermore, the diffusion of wearable inertial sensors is enabling novel ways of assessing balance in standing and gait.

A critical reading of the background literature in the sections above revealed some research gaps regarding the assessment of balance and fall risk in older adults. The first research gap concerns the use of wearable inertial sensors for instrumenting traditional functional balance tests (e.g. TUG test). These sensors can potentially provide an objective and accurate fall risk assessment, by producing detailed information on the timing and execution of functional tasks (e.g. standing and walking). However, some reviews on the topic have acknowledged an issue in the variety of sensor placements, functional tasks and measured variables that have been used in previous studies. This heterogeneity hinders a consensus on the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults. Therefore, the identification of an optimal protocol requires further research. This gap motivated the study presented in chapter 3.

The second research gap concerns the methods used to characterise posturography data, specially CoP time-series. For decades, global measures of CoP displacement have been used (e.g. total length, amplitude and standard deviation), which represents a linear analysis of the data. However, the diffusion of the dynamical systems theory within the biomedical research community has inspired the use of various quantitative descriptors of nonlinear dynamics. Among them, ApEn and SampEn have been proposed as a measure of body sway (ir)regularity. However, their ability to discriminate between groups with different fall risk and the suitable selection of the input parameters needed for their computation, have not yet been formally investigated. This gap motivated the study presented in chapter 4.

The third research gap is more concerned with the philosophy underlying current practices in fall risk assessment and prevention. As seen in this chapter, these practices focus on the occasional assessment of risk factors and changes in the balance control system that may lead to a fall (e.g. limited functional mobility and reduced visual acuity). Nevertheless, the dissemination of wearable technology is enabling the continuous monitoring of physiological and behavioural variables (e.g. heart rate and sleep patterns, respectively), which can be potentially used to infer health status and behaviours linked to impaired balance and increased risk of falling. Hence, these technologies could drive a shift to a new approach to fall prevention in vulnerable populations, i.e. one which includes the continuous monitoring and detection of short-lived factors that might result in an imminent fall. In particular, wearable technology offers new opportunities for in-home continuous sleep monitoring in a wider population (e.g. older adults living in long-term care

institutions). It is potentially relevant for fall prevention, given that chronic sleep disturbances and poor sleep quality are associated with future falls in older people. Hence, if short-lived sleep disturbances and poor sleep quality have a similar effect on balance control, continuous sleep monitoring would be relevant for fall prevention programmes in frail populations and sleep disturbance-inducing scenarios (e.g. hospital wards). Therefore, the potential association between day-to-day variations in sleep quality and balance control deficits warrants investigation. This gap motivated the study presented in chapter 5. Accordingly, the present chapter has also introduced the basic principles of sleep and its assessment, highlighting those that are relevant to this thesis (section 2.5).

The next chapters present the studies performed to address the above research gaps. As an ensemble, these studies aimed to expand the body of knowledge regarding the use of wearable sensors and nonlinear signal analysis methods for balance and fall risk assessment in older adults.

Chapter 3

Wearable Inertial Sensors for Fall Risk Assessment in Older Adults: a Systematic Review and Meta-Analysis

3.1 Chapter overview

Wearable inertial sensors can potentially provide an objective and accurate fall risk assessment based on detailed information on the timing and execution of functional tasks (e.g. standing and walking). However, some reviews on the topic have acknowledged an issue in the variety of sensor placements, movement tasks and measured variables that have been used in previous studies. This heterogeneity hinders a consensus on the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults. Therefore, the identification of an optimal protocol requires further research. This chapter presents a systematic review and meta-analysis performed in order to identify such a protocol, including optimal sensor placement, task and measured variables or features.

3.2 Introduction

Wearable inertial sensors are microelectronic devices that integrate accelerometers and gyroscopes in a small unit, enabling the continuous quantification of movements of the user during the execution of functional tasks (e.g. walking). More specifically, these sensors measure the linear acceleration and angular velocity of body segments,

from which a vast number of quantitative descriptors, or features, can be computed.

In the last two decades, the use of wearable inertial sensors for fall risk assessment has been on the rise. Researchers have used these sensors with the aim of producing instrumented functional balance tests [10, 12]. In their studies, subjects were asked to perform one or more movement tasks while wearing one or more inertial sensors on different body landmarks. Moreover, subjects at high risk of falling were identified based on retrospective fall history (i.e. self-reported previous falls), prospective fall occurrence, clinical assessment (e.g. a Timed-Up-and-Go test (TUG test)) or a combination thereof. This information and the features extracted from the recorded signals were later used to develop mathematical or statistical models for predicting future fall occurrence or classifying subjects into fall risk categories.

Some reviews on the topic have revealed a considerable heterogeneity between studies regarding the sensor placement, movement task, features and models used for the development of sensor-based fall risk assessment tools [10–12]. This heterogeneity precludes any firm conclusions on the optimal wearable inertial sensor-based protocol for assessing fall risk.

This chapter presents an original systematic review and meta-analysis performed to synthesise the empirical evidence related to the use of inertial sensors for fall risk assessment and prediction in generally healthy older adults ($\geq$60 years old with no medical history of neurological, neurodegenerative, cognitive or motor problems), in order to identify the optimal combination of sensor placement, movement task and measured variables or features. The identification of such a protocol should contribute to closing the gap between research studies and clinical applications, by enabling the evidence-based design of new studies and real-life applications. The contents of this chapter have been published elsewhere [128].

3.3 Methods

3.3.1 Search strategy

Potentially relevant articles were identified through a literature search in PubMed, EMBASE, IEEEXplore, Cochrane Central Register of Controlled Trials (CENTRAL), ClinicalTrials.gov and the World Health Organization (WHO) International Clinical Trials Registry Platform electronic databases.

Articles were searched using Boolean combinations of the following keywords or equivalent Medical Subject Heading (MeSH) terms: accidental falls AND (risk assessment OR prediction) AND (sensor OR device OR wearable OR technology).

Additional papers were identified from the references of relevant review articles previously published [10, 11, 54].

Papers were considered suitable for this review if they met these inclusion criteria:

1. Original peer-reviewed journal articles published between January 2006 and December 2016;

2. Studies in which the subjects were labelled as fallers and non-fallers (alternatively, high and low fall-risk), based on retrospective fall history, prospective fall occurrence, clinical assessment (e.g. TUG test) or a combination thereof;

3. A sample of at least ten subjects with an average age of 60 or over;

4. Body-worn inertial sensors were used to characterise a functional task (e.g. walking) by extracting features from the recorded signals, and;

5. Group statistics, specifically mean and standard deviation, for sensor-based features, as well as the statistical significance level for the difference between groups were reported.

Papers were excluded if they reported studies focused on patients suffering from neurological, neurodegenerative, cognitive or motor problems (e.g. stroke, Parkinson's disease, dementia and osteoarthritis, respectively), since this review was focussed on generally healthy older adults.

3.3.2 Paper selection and data extraction

Database records responding to the selected keywords were identified following the search strategy described above. After excluding duplicates (i.e. titles indexed in more than one database), studies were shortlisted based on the inclusion and exclusion criteria by screening titles, abstracts and full-texts.

Subsequently, relevant data were extracted from the shortlisted studies; namely: first author and year of publication; number of participants and proportion of fallers; subject labelling method with details (e.g. the duration of follow-up period when prospective fall occurrence was used); type, quantity and placement of inertial sensors; functional task or test characterised using sensor-based features (e.g. walking or the TUG test, respectively).

Finally, a listing of features reported in the shortlisted studies was compiled to enable further statistical analysis. For each feature the following items were included: name and category (i.e. linear acceleration, angular velocity, temporal,

spatial, frequency, or nonlinear features [10]), units, mean and standard deviation for each group (i.e. on-fallers and fallers), and trend of the difference between groups. A trend was represented with two arrows, $\downarrow\downarrow$ (or $\uparrow\uparrow$), if the mean value of a feature significantly (p-value$<$0.05) decreased (increased) for fallers compared to the mean value for non-fallers. Similarly, one arrow, $\downarrow$ (or $\uparrow$), was used if the mean value of a feature non-significantly (p-value$>$.05) decreased (increased) for fallers compared to the mean value for non-fallers. Sensor placement and functional task for each feature were also included in the listing.

3.3.3 Statistical analysis of sensor-based features

Standard methods for the analysis of categorical data were applied on the feature listing with two objectives [129, 130]: 1) to investigate the level of association between trend significance status (i.e. non-significant or significant) and feature category, sensor placement and task, and; 2) to identify optimal triads of feature category, sensor placement and task.

Firstly, Pearson's chi-squared tests were performed in order to prove the association between trend significance status (dependent variable) and feature category, sensor placement and task (covariates). In other words, the aim was to prove that significant feature trends are dependent on feature category, sensor placement and task. A p-value$<$0.05 was accepted as statistically significant evidence of a nonrandom association. Moreover, Pearson's Contingency (C) and Cramer's (V) coefficients were computed in order to quantify the level of association between each covariate and trend significance status. A C (V) coefficient of 0.1 (0.1), 0.287 (0.3) and 0.447 (0.5) was considered as evidence of small, medium and large level of association, respectively [131].

Secondly, significant triads of feature category, sensor placement and task were identified as follows. A three-way contingency table containing the covariates above was created using the subset of features containing only significant trends. Pearson's residuals were computed for each triad in the table and used to characterise the strength (value) and nature (sign) of association for each triad. Large positive residuals are obtained when the observed frequency of significant features is substantially higher than the expected frequency, which would suggest significant features were more likely to arise from that specific triad. Conversely, large negative residuals are obtained when the observed frequency of significant features is substantially lower than the expected, which would suggest significant features were less likely to arise from that specific triad. For interpretability, the following representation was used to report the results (instead of numerical values): two ar-

rows, ↓↓ (or ↑↑), if the residuals were smaller (or larger) than -4 (or +4), revealing strong associations; one arrow, ↓ (or ↑), if the residuals were smaller (or larger) than -2 (or +2), revealing medium-associations, and; a dash, -, for residuals greater than or equal to -2 but smaller than or equal to +2, revealing weak associations. These thresholds are customarily used in the interpretation of Pearson residuals as a measure of the strength of association [130]. A Pearson's chi-squared test of independence was performed to confirm the statistical significance of those associations (p-value<0.05).

The software R version 3.2.3 was used to perform this analysis. The source code can be found in Appendix A.

3.3.4 Meta-analysis of sensor-based features

A meta-analysis of the features extracted from the shortlisted studies was conducted to calculate the pooled difference between groups (fallers - non-fallers), as well as the statistical significance of these differences. Features were included in the meta-analysis if [the feature was reported in at least two studies] AND [the feature was computed for the same task/subtask] AND [the sensor placement and type were the same across studies OR feature was independent of the sensor placement and type (e.g. number of steps or stride time)]. Standard methods for combining and reporting continuous outcomes were employed to pool the features [132]: pooled sample size, Mean Difference (MD) with Confidence Interval at 95% (CI), and statistical significance level (p-value). MD and CI were considered significant if the p-value $<$ 0.05.

Random or fixed effect models were selected based on the heterogeneity between studies, assessed using the Q-statistic (computed via a Chi-squared test) and the I^2 statistic. A significant Q-statistic is indicative of dissimilar effect sizes across studies; a threshold significance level of 0.1 was selected as statistically significant value as suggested in [132]. The I^2 statistic indicates the percentage of the variability in effect sizes due to heterogeneity across studies, and not due to sampling error within studies. An I^2 value from 30% to 60%, 50% to 90% and 75% to 100% represent moderate, substantial and considerable heterogeneity, respectively.

The R package meta_4.8-4 was used to perform the meta-analysis [133]. The default options for both fixed and random effects models were used; i.e. the inverse variance method for study weighting and the DerSimonian-Laird estimate for the random effects model [134]. The source code can be found in Appendix A.

3.3.5 Quality appraisal of selected studies

The methodological quality of the selected studies was assessed using the checklist provided in Appendix B. This checklist was adapted from [135]. It contains 15 questions that are scored *yes* or *no/unclear*. These questions are organised in 3 dimensions:

- Reporting (11 items) which assessed whether the information provided in the paper was clear and sufficient to replicate the study and appraise its validity.
- External validity (2 items) which addressed the extent to which the findings of the study could be generalised to a broader population and context.
- Internal validity (2 items) which assessed whether the evidence at hand suggests that the study was designed and conducted to minimise bias and confounding.

A summary of the main findings is provided below in an attempt to reveal the methodological issues that future studies in the field should address in order to produce more robust scientific evidence.

3.4 Results

Based on the search strategy described above, 481 records were identified through a database search and 18 through a linear search. After removing 51 duplicates, 448 titles were screened by title and 257 were excluded as they did not meet the inclusion/exclusion criteria. From the remaining 191 titles, 127 were removed after screening the abstract against inclusion/exclusion criteria, which left 64 papers to be read in full-text. After reading the full-texts, 51 were excluded due to the inclusion/exclusion criteria. Therefore, 13 studies were shortlisted for this review [136–148]. A flowchart of the study selection process is shown in Figure 3.1.

Importantly, there were some papers among the excluded ones which are noteworthy for the novelty of their approach to the problem, but that failed to meet inclusion criterion 5. In particular, the studies by Toebes *et al.* [55] and Riva *et al.* [149] found significant associations between fall risk and nonlinear descriptors of gait dynamics (e.g. Multi-scale Entropy (MSE) and Recurrence Quantification Analysis (RQA) measures). Moreover, Rispens *et al.* [150] and van Schooten *et al.* [56, 151] found significant associations between fall risk and ambulatory gait measures of quantity and quality.

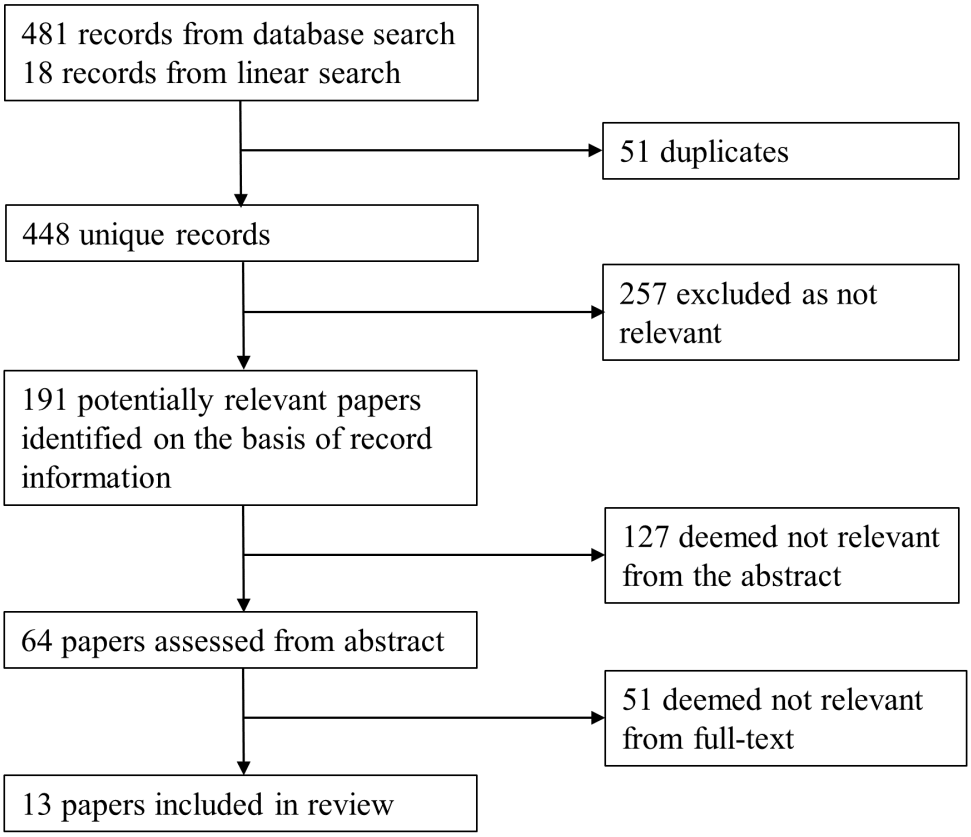

Figure 3.1: Flowchart of study selection. The 13 selected papers were original peer-reviewed journal articles published between January 2006 and December 2016. These papers reported studies with a minimum sample size of 10 subjects (mean age $\geq$ 60 years), who were labelled as fallers and non-fallers based on retrospective fall history, prospective fall occurrence, clinical assessment or a combination thereof. Body-worn inertial sensors were used to characterise a functional task (e.g. walking), and the mean and standard deviation for each sensor-based measure was reported.

3.4.1 Characteristics of selected studies

The 13 studies enrolled from 17 to 349 subjects each (mean ± standard deviation: 93.15 ± 86.18 subjects), for a cumulative population of 1,211. Overall, the studies included 565 faller subjects, i.e. 47% of the cumulative population. However, this proportion ranged from 14 to 71% across the 13 selected studies. The majority of studies (92%) enrolled both men and women, except for one study which enrolled only women [139]. Subjects were enrolled in a clinic as part of a larger clinical research project in 4 studies [138, 141, 142, 145], in a community centre in one study [146], in a hospital's physiotherapy service in one study [137], and via a letter sent to members of the community in one study [139]; details about the recruitment process were not provided in six studies [136, 140, 143, 144, 147, 148]. Additional details about the shortlisted studies are reported in Table 3.1.

Subjects were labelled as (non-)fallers using retrospective fall history in ten studies, with a recall period of one year for eight studies and five years for two studies; prospective fall occurrence through a one-year follow-up period in two studies; and a clinical assessment (i.e. the Tinetti scale [76]) in one study.

Tri-axial accelerometers and gyroscopes were the only types of inertial sensor used in 10 studies and one study respectively; a combination of sensors was used in two studies. In seven studies only one sensor was used, in five studies two sensors were used, and one study used four sensors.

The most common sensor placement was the lower back (i.e. approximately on the L3 vertebra) with ten studies, followed by shins (i.e. frontal middle point between the knee and the foot) and feet (i.e. dorsal part of the foot) with two studies each. Other placements were knee, ankle, thigh, sternum and upper back (i.e. approximately on the C7 vertebra), with one study each. When grouping placements into upper body (trunk) and lower body (lower limbs), there were eleven (91.7%) and seven (58.3%) studies, respectively.

Inertial signals were acquired during the following tasks: walking other than a standardised test (7 studies), unperturbed standing (three studies), the TUG test (two studies), the 10-Meters-Walking test (10MW test) (one study), and the Five-Times-Sit-to-Stand test (FTSS test) (one study). A brief description of these tasks is presented in table 3.2; for a more detailed description, the reader may refer to the referenced paper.

Table 3.1: Characteristics of selected studies

Study	Subjects (Fallers)	Age, years Mean (SD)	Fall ascertainment method	Type of sensor	Quantity	Placement	Task
[136]	153 (22)	71.0 (7.7)	Retrospective falls	Accelerometer	1	Lower back	Walking
[137]	17 (12)	77.0 (7.5)	Retrospective falls	Accelerometer	1	Lower back	Standing
[138]	349 (207)	72.4 (7.4)	Retrospective falls	Gyroscope	2	Shins	TUG test
[139]	97 (54)	68.7 (7.1)	Prospective falls	Accelerometer	2	Feet	Walking
[140]	41 (23)	78.2 (6.2)	Retrospective falls	Accelerometer	1	Lower back	TUG test
[141]	40 (19)	71.4 (7.3)	Retrospective falls	Accelerometer & gyroscope	2	Lower back & shins	Standing & Walking
[142]	120 (65)	73.7 (5.8)	Retrospective falls	Accelerometer & gyroscope	1	Lower back	Standing
[143]	30 (7)	75.0 (5.7)	Retrospective falls	Accelerometer	4	Lower back, knee, foot	Walking
[144]	100 (50)	76.5 (5.7)	Clinical assessment	Accelerometer	1	Lower back	Walking
[145]	39 (19)	71.5 (6.6)	Retrospective falls	Accelerometer	2	Upper leg & sternum	FTSS test
[146]	73 (16)	80.7 (7.8)	Prospective falls	Accelerometer	2	Lower & upper back	10MW test
[147]	71 (32)	78.4 (4.7)	Retrospective falls	Accelerometer	1	Lower back	Walking
[148]	81 (39)	78.4 (4.8)	Retrospective falls	Accelerometer	1	Lower back	Walking

TUG test timed up and go test, *10MW test* 10-metre walk test, *FTSS test* five-times-sit-to-stand test, *SD* standard deviation

Table 3.2: Description of tasks

Task	Description
Walking	Participants were instructed to walk: • 8–10 steps at comfortable and maximum speeds along a straight course [136] • 7 minutes at self-selected speed around a continuous walking circuit [139] • 3 metres at comfortable speed along a straight course [141] • 10 metres at a self-selected speed along a straight course which included stepping over six obstacles separated by 1.5 metres [143] • 20 metres at self-selected speed on a straight course and back to the starting point [144] • 1 minute or longer walking bouts during daily life activities [147] • 1 minute under three different conditions: 1) baseline, usual walk; 2) baseline, usual walk with harness; 3) an obstacle course walk with harness [148]
Unperturbed standing	Participants were instructed to stand still: • 30 seconds on a rigid surface with eyes open and eyes closed, as well as on a mat with eyes open and closed [137, 141] • 40 seconds with eyes open in a semi-tandem stance and 30 seconds with eyes closed [142]
TUG test	Participants were instructed to rise from a chair, walk 3 metres at a comfortable speed on a straight course, turn around, walk back to the chair and sit down [138, 140]
10MW test	Participants were instructed to walk at comfortable speed along a 10-metres straight course [146]
FTSS test	Participants were instructed to keep their arms folded across their chest for the duration of the test and to fully stand up and sit back down five times as quickly as possible [145]

TUG test timed up and go test, *10MW test* 10-metre walk test, *FTSS test* five-times-sit-to-stand test

3.4.2 Sensor-based features and their trends

The full listing of features extracted from the inertial sensors that were reported in the 13 selected papers was published elsewhere as supplementary material [128]. Green *et al.* [138] reported features for all of the subjects included in their analysis as well as for some subgroups separately (i.e. males, females < 75 years old and females ≥ 75 years old). However, only the results for all the subjects were included in this review. Moreover, Doheny *et al.* [141] performed an instrumented gait assessment four times in the same day. However, only the results of the first assessment (between 9:00 and 9:30 a.m.) were included in the review.

In summary, 93 distinct features were identified in the selected studies and categorised as suggested elsewhere [10]: linear acceleration (15 features, 16.1%), angular velocity (28 features, 30.1%), spatial (four features, 4.3%), temporal (24 features, 25.8%), frequency (21 features, 22.6%) and nonlinear (one feature, 1.1%).

These features were reported 175 times in the selected studies out of which for 84 times (48%) they exhibited a significant trend. Table 3.3 summarises the frequency of features per task, sensor placement and feature category for the complete listing of features and the subset of features showing significant trends.

3.4.3 Statistical analysis of sensor-based features

The results from the Pearson's chi-squared tests and the measures of association revealed statistically significant associations between feature significance and feature category, sensor placement and task (Table 3.4).

Furthermore, the computed Pearson's residuals for the three-way table containing feature category, task and sensor placement as covariates revealed strong to very strong associations for nine triads. Table 3.5 summarises these results. As an example, the double arrow, ↑↑, for the triad 'angular velocity-walking-shins' means that significant features are much more likely to arise from this combination. Conversely, the single arrow, '↓', for the triad 'angular velocity-walking-lower back' means that significant features are less likely to arise from this combination. The '-' symbol indicates that the significance of a feature is not particularly affected by its category, sensor placement or task.

3.4.4 Meta-analysis of sensor-based features

Based on the selection criteria for the meta-analysis, 20 features were pooled using the methods described above. Table 3.6 shows the trend and values for those features, as well as the number of subjects in each group. It also shows the task and

Table 3.3: Frequency table for features by task, sensor placement and feature category. The first two columns are the frequency and percentage of features per task, sensor and category for all the sensor-based features reported in the selected studies. The second two columns are the frequency and percentage of features per task, sensor and category for features that showed differences between non-fallers and fallers.

	All features (n = 175)		Significant features (n = 84)	
	Count	%	Count	%
Task				
Walking [a]	110	62.9	61	72.6
Unperturbed standing	48	27.4	15	17.8
Sit-to-stand/Stand-to-sit [b]	14	8	5	6
TUG test	3	1.7	3	3.6
Sensor placement				
Lower back	98	56	49	58.3
Shins	60	34.3	33	39.3
Foot	7	4	0	0
Sternum	4	2.3	0	0
Upper back	3	1.7	2	2.4
Knee	3	1.7	0	0
Feature category				
Linear acceleration	48	27.4	20	23.8
Temporal	45	25.7	19	22.6
Frequency	42	24	16	19
Angular velocity	32	18.3	25	29.8
Spatial	7	4	4	4.8
Nonlinear	1	0.6	0	0

[a] Including the walking part of a functional test (e.g. TUG test)
[b] Including sit-to-stand/stand-to-sit transitions being part of a functional test (e.g. TUG test)
TUG test timed up and go test

Table 3.4: Measures of association between feature significance and covariates. The level of association describes the extent to which the significance of the difference between non-fallers and fallers depends on the task, sensor placement and feature category.

Covariate	χ^2	p-value	C	V	Association level [a]
Task	11.94	**<0.01**	0.253	0.261	Medium
Sensor placement	14.68	**0.01**	0.278	0.29	Medium
Feature category	15.82	**<0.01**	0.288	0.301	Medium

χ^2 Pearson's chi-squared statistic for the association test in which the null hypothesis is no association, C Pearson's contingency coefficient, V Cramer's coefficient.
[a] A C (V) of 0.100 (0.1), 0.287 (0.3) and 0.447 (0.5) are considered as evidence of small, medium and large association, respectively

Table 3.5: Association trend. The association trend describes the extent to which the significance of the difference between non-fallers and fallers depends on a specific combination of task, sensor placement, and feature category. Combinations producing double upward arrows should be favoured in sensor-based fall risk assessment protocols.

Feature category	**Task**: Unperturbed standing	FTSS test	TUG test	Walking	**Sensor placement**
Angular velocity	-	-	-	↓	LB
	-	-	-	↑↑	Shins
	-	-	-	-	UB
Frequency	-	-	-	↑	LB
	-	-	-	↓	Shins
	-	-	-	↑	UB
Linear acceleration	↑↑	↑↑	-	-	LB
	-	-	-	↓	Shins
	-	-	-	-	UB
Spatial	-	-	-	-	LB
	-	-	-	-	Shins
	-	-	-	-	UB
Temporal	-	-	-	-	LB
	-	-	↑	-	Shins
	-	-	-	-	UB

FTSS test five-times-sit-to-stand test, *TUG test* timed up and go test, *LB* lower back, *UB* upper back
↓↓ (↑↑): substantially stronger negative (positive) association for a specific triad of feature category, task and sensor placement
↓ (↑): strong negative (positive) association for a specific triad of feature category, task and sensor placement
-: non-significant association for a specific triad of feature category, task and sensor placement

the sensor placement for each feature.

Linear acceleration features included in the meta-analysis were: Root Mean Square (RMS) value (expressed in g-force units) of the acceleration signal in the Medial-Lateral (ML) direction assessed at the lower back during unperturbed standing with both eyes open and eyes closed (ML RMS of acceleration). This feature is related to postural stability during standing.

Spatial features included in the meta-analysis were: the number of steps during the TUG test, and step length estimated from inertial signals measured during the walking stage of the TUG test or another walking task.

Temporal features included in the meta-analysis were: cadence (i.e. steps per minute); gait speed; step time; stance time; swing time; stride time; total time to complete the TUG test; single and double support time, i.e. the time during which only one foot and both feet are in contact with the walking surface, respectively, expressed as a percentage of a gait cycle; and the Coefficient of Variation (CV) for step, stance, swing, stride, single and double support times. The CV is the ratio of the standard deviation to the mean for a given feature, expressed as a percentage; hence, it is a standardised measure of dispersion of the distribution of feature values.

All the spatial and temporal features included in the meta-analysis are widely used in clinical gait analysis [53].

One frequency feature was included in the meta-analysis: the Harmonic Ratio of trunk acceleration in the vertical direction. The Harmonic Ratio has been defined as the ratio of even to odd signal harmonics extracted from the spectrum of the acceleration signal and has been suggested as a measure of the stability and smoothness of trunk movement during gait [146].

Neither angular velocity nor non-linear features were included in the meta-analysis, as none of them met the criteria to be pooled; i.e. either they were reported only in one study or they were measured during different tasks or at different sensor body placements.

The relative pooling weight of each study is reported in Table 3.6. The results of the pooling are reported in Table 3.7, where also the trend of the pooled features is shown.

Four out of twenty pooled features showed a statistically significant difference between fallers and non-fallers. Namely, fallers exhibited:

- A higher RMS value for the ML acceleration during unperturbed standing with eyes closed (MD: 0.01 g; CI: 0.006–0.014; $p<0.01$)
- A higher number of steps to complete the TUG test (MD: 1.638 steps; CI:

0.384–2.892; p=0.01)

- A longer time to complete the TUG test (MD: 2.274 seconds; CI: 0.531–4.017; p<0.01)
- A longer step time during walking (MD: 0.053 seconds; CI: 0.012–0.095; p=0.01)

3.4.5 Quality appraisal of selected studies

All the studies reported the aim of the study, experimental protocol (i.e. task, sensor quantity and placement), technical specifications of the sensor, methods for signal processing, feature extraction and statistical analysis, and features' summary statistics per group (non-fallers and fallers). However, only seven studies reported actual p-values (e.g. 0.035 rather than <0.05) for the differences between groups [137, 140, 144–148].

Moreover, only seven studies reported inclusion and exclusion criteria of participants and the distribution of potential confounders per group (e.g. age and comorbidities) [139, 140, 142, 144, 146–148]. Therefore, the internal validity of six studies remains unclear, since unreported (or unobserved) variables could explain feature differences between fallers and non-fallers.

Finally, external validity was found for all shortlisted studies, since their samples were representative of the population under investigation and the task was representative of clinical fall-risk assessment protocols or daily-life activities.

Table 3.6: Sensor-based features included in the meta-analysis

Feature	Study	Task	Sensor placement	Trend	Weight (%)	Non-Fallers N	Non-Fallers Mean (SD)	Fallers N	Fallers Mean (SD)
Linear acceleration features									
ML RMS acceleration (g)	[141]	Unperturbed standing (EO)	Lower back	-	50.7	21	0.03 (0.01)	19	0.03 (0.01)
	[142]	Unperturbed standing (EO)	Lower back	↑↑	49.3	55	0.04 (0.01)	65	0.06 (0.03)
ML RMS acceleration (g)	[141]	Unperturbed standing (EC)	Lower back	↑↑	44.3	21	0.03 (0.01)	19	0.04 (0.01)
	[142]	Unperturbed standing (EC)	Lower back	↑	55.7	55	0.04 (0.01)	65	0.05 (0.02)
Spatial features									
Number of steps (steps)	[140]	TUG test (Walking)	Lower back	↑	43.6	18	10.61 (1.80)	23	11.52 (1.82)
	[138]	TUG test (Walking)	Shins	↑↑	56.4	142	10.60 (2.40)	207	12.80 (3.80)
Step length (m)	[140]	TUG test (Walking)	Lower back	↓	49.8	18	0.56 (0.08)	23	0.53 (0.08)
	[144]	Walking	Lower back	↑↑	50.2	50	0.51 (0.13)	50	0.66 (0.09)
Temporal features									
Cadence (steps/min)	[138]	TUG test (Walking)	Shins	↓↓	50.2	142	108 (19.3)	207	99.2 (19.3)
	[144]	Walking	Lower back	↑↑	49.8	50	101.4 (13.8)	50	111.6 (10.2)
Gait speed (m/s)	[146]	10MW test	Lower back	↓↓	32.3	57	0.98 (0.34)	16	0.63 (0.27)
	[140]	TUG test (Walking)	Lower back	↓↓	34.1	18	0.68 (0.10)	23	0.60 (0.09)
	[144]	Walking	Lower back	↑↑	33.6	50	0.86 (0.26)	50	1.23 (0.22)
Step time (s)	[138]	TUG test (Walking)	Shins	↑↑	26.5	142	0.60 (0.10)	207	0.70 (0.10)
	[140]	TUG test (Walking)	Lower back	↑↑	23.8	18	0.50 (0.06)	23	0.56 (0.05)
	[147]	Walking	Lower back	↑↑	25	39	0.56 (0.04)	32	0.60 (0.07)
	[141]	Walking	Shins	↑	24.6	21	0.57 (0.05)	19	0.58 (0.05)
Stance time (s)	[138]	TUG test (Walking)	Shins	-	71.1	142	0.80 (0.20)	207	0.80 (0.10)
	[141]	Walking	Shins	↑	28.9	21	0.68 (0.10)	19	0.70 (0.08)
Swing time (s)	[138]	TUG test (Walking)	Shins	-	96.3	142	0.50 (0.10)	207	0.50 (0.10)
	[141]	Walking	Shins	↓	3.7	21	0.47 (0.25)	19	0.43 (0.04)

Table 3.6 continued from previous page

Feature	Study	Task	Sensor placement	Trend	Weight (%)	Non-Fallers		Fallers	
						N	Mean (SD)	N	Mean (SD)
Stride time (s)	[138]	TUG test (Walking)	Shins	-	51.6	142	1.20 (0.20)	207	1.20 (0.20)
	[147]	Walking	Lower back	↓↓	28.2	39	1.12 (0.09)	32	1.20 (0.15)
	[141]	Walking	Shins	↑	20.2	21	1.11 (0.11)	19	1.13 (0.11)
Total time (s)	[140]	TUG test	Lower back	↑↑	52	18	8.68 (1.62)	23	10.10 (1.61)
	[138]	TUG test	Shins	↑↑	48	142	12.4 (5.1)	207	15.6 (6.5)
Single support time (%)	[138]	TUG test (Walking)	Shins	-	68.9	142	80 (10)	207	80 (10)
	[141]	Walking	Shins	↓↓	31.1	21	78.39 (5.59)	19	75.53 (4.67)
Double support time (%)	[138]	TUG test (Walking)	Shins	↓↓	55.4	142	50 (20)	207	40 (20)
	[141]	Walking	Shins	↓	44.6	21	24.67 (17.08)	19	24.47 (4.67)
CV step time (%)	[138]	TUG test (Walking)	Shins	↑	43.3	142	40.3 (22.9)	207	42 (21)
	[141]	Walking	Shins	↑	56.7	21	4.92 (4.39)	19	6.20 (8.18)
CV stance time (%)	[138]	TUG test (Walking)	Shins	↓	65.6	142	45 (20.4)	207	43.3 (19.3)
	[141]	Walking	Shins	↑	34.4	21	6.03 (8.67)	19	7.40 (10.16)
CV swing time (%)	[138]	TUG test (Walking)	Shins	↓	43	142	31 (22)	207	28.1 (19.9)
	[141]	Walking	Shins	↑↑	57	21	5.06 (2.97)	19	7.26 (4.94)
CV stride time (%)	[138]	TUG test (Walking)	Shins	↑	58.8	142	23.4 (14.7)	207	24 (13.2)
	[141]	Walking	Shins	↑	41.2	21	4.19 (5.56)	19	4.96 (6.01)
CV single support time (%)	[138]	TUG test (Walking)	Shins	↑	38.8	142	21.10 (19.20)	207	22.90 (15.70)
	[141]	Walking	Shins	↑	61.2	21	4.08 (4.51)	19	5.41 (5.21)
CV double support time (%)	[138]	TUG test (Walking)	Shins	↓	52.6	142	82.60 (27.80)	207	80.70 (26.60)
	[141]	Walking	Shins	↑	47.4	21	10.02 (9.61)	19	16.54 (12.39)

Table 3.6 continued from previous page

Feature	Study	Task	Sensor placement	Trend	Weight (%)	Non-Fallers N	Non-Fallers Mean (SD)	Fallers N	Fallers Mean (SD)
Frequency features									
VT Harmonic ratio	[146]	10MW test	Lower back	↓↓	50.3	57	2.69 (0.93)	16	2.07 (0.64)
	[144]	Walking	Lower back	↑↑	49.7	50	2.18 (1.09)	50	3.09 (1.25)

SD standard deviation, *RMS* root mean square, *CV* coefficient of variation, *ML* medial-lateral, *VT* vertical, *EO* eyes open, *EC* eyes closed, *TUG test* timed up and go test, *10MW test* 10-metre walk test

↓↓ (↑↑): significantly lower (higher) for subjects in the fallers group

↓ (↑): lower (higher) for subjects in the fallers group

-: no difference between groups

Table 3.7: Pooled sensor-based features. Four pooled features showed significant differences between non-fallers and fallers.

	Heterogeneity					Weighted Mean Difference			
Feature	I^2 (%)	Q	p-value	Model	Subjects	MD	CI	p-value	Trend
Linear acceleration features									
ML RMS of acceleration, EO (g)	93.6	15.57	<0.010	Random	160	0.010	(-0.001; 0.030)	0.32	↑
ML RMS of acceleration, EC (g)	0	0	1	Fixed	160	0.010	(0.006; 0.014)	**<0.01**	↑↑
Spatial features									
Number of steps (steps)	73.9	3.83	0.05	Random	390	1.638	(0.384; 2.892)	**0.01**	↑↑
Step length (m)	96.5	28.58	<0.01	Random	141	0.060	(-0.116; 0.237)	0.50	↑
Temporal features									
Cadence (steps/min)	97.1	35.01	<0.01	Random	449	0.661	(-17.958; 19.281)	0.94	↑
Gait speed (m/s)	97.6	84.47	<0.01	Random	214	-0.016	(-0.376; 0.345)	0.93	↓
Step time (s)	88.1	25.18	<0.01	Random	501	0.053	(0.012; 0.095)	**0.01**	↑↑
Stance time (s)	0	0.35	0.55	Fixed	389	0.006	(-0.024; 0.036)	0.71	↑
Swing time (s)	0	0.50	0.48	Fixed	389	-0.002	(-0.022; 0.020)	0.89	↓
Stride time (s)	57.3	4.68	0.09	Fixed	460	0.026	(-0.004; 0.057)	0.09	↑
Total time (s)	79.6	4.91	0.03	Random	390	2.274	(0.531; 4.017)	**<0.01**	↑↑
Single support time (%)	53.3	2.14	0.14	Fixed	389	-0.888	(-2.662; 0.885)	0.33	↓
Double support time (%)	79.4	4.85	0.03	Random	389	-5.625	(-15.174; 3.924)	0.25	↓
CV step time (%)	0	0.02	0.9	Fixed	389	1.462	(-1.649; 4.572)	0.36	↑
CV stance time (%)	0	0.69	0.41	Fixed	389	-0.643	(-4.095; 2.809)	0.71	↓
CV swing time (%)	73	3.70	0.05	Random	389	0.005	(-4.945; 4.954)	1	↑
CV stride time (%)	0	0.01	0.94	Fixed	389	0.670	(-1.641; 2.981)	0.57	↑
CV single support time (%)	0	0.04	0.85	Fixed	389	1.512	(-0.863; 3.887)	0.21	↑
CV double support time (%)	69.9	3.32	0.07	Random	389	2.095	(-6.146; 10.336)	0.62	↑

Table 3.7 continued from previous page

	Heterogeneity					Weighted Mean Difference			
Feature	I^2 (%)	Q	p-value	Model	Subjects	MD	CI	p-value	Trend
Frequency features									
VT harmonic ratio	95.9	24.44	<0.01	Random	173	0.140	(-1.359; 1.640)	0.85	↑

CI 95% confidence interval, *RMS* root mean square, *CV* coefficient of variation, *ML* medial-lateral, *VT* vertical, *EO* eyes open, *EC* eyes closed

↓↓ (↑↑): significantly lower (higher) for subjects in the fallers group

↓ (↑): lower (higher) for subjects in the fallers group

3.5 Discussion

This study analysed the scientific literature focusing on the use of wearable inertial sensors for the risk of fall assessment and prediction, exploring the sensitivity of sensor-based features to sensor placement, functional task and feature category.

The statistical analysis of features reported in the 13 shortlisted studies revealed significant, very strong, positive associations in three different triads of feature category, task, and sensor placement:

- Angular velocity - Walking - Shins
- Linear acceleration - Unperturbed standing - Lower back
- Linear acceleration - Stand to sit/Sit to stand - Lower back

These results suggested that these are optimal combinations when using inertial sensors to discriminate between fallers and non-fallers. Other potentially suitable combinations, given their strong, positive associations are:

- Frequency - Walking - Lower back
- Frequency - Walking - Upper back
- Temporal – TUG test - Shins

Conversely, the findings suggest that the use of the following combinations should be avoided as they are less discriminative of fall risk:

- Angular velocity - Walking - Lower back
- Frequency - Walking - Shins
- Linear acceleration - Walking - Shins

Further multivariate analyses can potentially reveal optimal combinations that include other factors, such as age and gender of the subjects. However, this would require more studies to be included in the analysis.

Moreover, the results of the meta-analysis demonstrated that four features are significantly higher in fallers than in non-fallers ($p<0.05$): the RMS acceleration in the medial-lateral direction during unperturbed standing with eyes closed (MD: 0.01 g; CI: 0.006–0.014); the number of steps (MD: 1.638 steps; CI: 0.384–2.892) and total time (MD: 2.274 seconds; CI: 0.531–4.017) to complete the TUG test; and the

step time (MD: 0.053; CI: 0.012–0.095) during walking. These results suggest that these combinations of task and features may be more suitable for fall risk assessment.

Additionally, five features exhibited a consistent trend across the selected studies. These features were: step time, CV for step time, CV for stride time and CV for single support time, which showed a higher value in fallers than in non-fallers; and double support time, which showed a lower value for fallers. However, these trends were not found to be statistically significant when pooled in the meta-analysis. This may be explained by the high values of standard deviation reported in the study by Green *et al.* [138], which was included in the pooling of these features. No clear explanation for such variability within that study can be inferred from the paper.

In contrast, seven features showed an inconsistent trend across the selected studies: step length, cadence, gait speed, harmonic ratio in the vertical direction, CV for stance time, CV for swing time, and CV for double support time. Importantly, in four features the methods used to classify subjects as (non-)fallers were also inconsistent between studies: step length and cadence were pooled from [140] and [144], in which the classification methods were retrospective fall history and clinical assessment, respectively. Although both studies scored high in terms of quality, there is additional evidence supporting the results provided by Weiss *et al.* [140]. Namely, in a study by Kwon *et al.* a significantly shorter step length was observed in fallers [152]. Gait speed was pooled from [140, 144, 146], with the latter adding prospective fall occurrence to the diversity of classification methods. Nevertheless, both Weiss *et al.* and Doi *et al.* reported a similar trend (i.e. a significantly lower gait speed in fallers), which renders their results more reliable [140, 146]. Finally, the harmonic ratio in the vertical direction was also pooled from [144, 146], combining subjects labelled as fallers using two different methods. Both studies scored high in terms of quality. Nevertheless, the study by Kwon *et al.* also provides supporting evidence to the significantly lower harmonic ratio reported by Doi *et al.* [146, 152]. The potential sources of between-study heterogeneity, revealed by the above trend inconsistencies, can potentially be further explored using quantitative approaches (e.g. subgroup analysis by study and patient characteristics). Unfortunately, the low number of studies reporting on the same feature rendered it unfeasible to apply these approaches.

Moreover, five features showed an ambiguous trend across the selected studies, as they were reported with no mean difference between non-fallers and fallers in one study while exhibiting a trend (significant or not) in another study. These features were: the RMS value of the acceleration in the medial-lateral direction with

eyes open, and stance time, swing time, stride time, and single support time during walking.

Altogether, the evidence synthesised in this review suggests that the instrumented TUG test is a suitable tool for discriminating non-fallers and fallers, provided that the inertial sensors are placed on the shins and angular velocity, temporal (e.g. total time and step time) and spatial (e.g. number of steps) features are computed. Additionally, the triad linear acceleration - unperturbed standing - lower back seems to be a suitable choice as well.

Nevertheless, it should be stressed that these results are limited, as they are based only on features reported in the 13 papers included in the review. Hence, they are unable to provide a representative inference of all features used and all studies published, but not included in the review. This means that there might be some other sensor-based features that are discriminant between non-fallers and fallers but which were not included in this systematic review as they were not reported as required by the inclusion criteria. This may be the case for some of the features reported in [55, 56, 149–151]. Relaxing the inclusion criteria could have increased the number of studies included in this study (e.g. including studies focused on falls in neurological patients as well) but at the risk of increasing the between-study heterogeneity.

Finally, a comment regarding heterogeneity in hit rate (i.e. the ratio of all features to significant features expressed as a percentage) reported in the selected studies is deemed relevant to this study. In some studies reporting a relatively high number of features (i.e. 28 or more) a hit rate ranging from 25 to 66% was achieved [138, 141, 142]. In contrast, some studies reporting a low number of features (i.e. seven or less) achieved hit rates above 85%, with two studies reporting a surprising 100% [144, 146, 148]. From these studies, it was not clear if the authors investigated a low number of features or if they investigated a large number of features but only reported the most significant ones. Even if reporting bias (a.k.a. selective reporting) should not be concluded from this finding, it should at least arise awareness of the potential presence of this practice in the biomedical engineering field. This practice could undermine the findings of future studies, making it more difficult to converge to meaningful conclusions.

3.6 Conclusions

This chapter presented an original systematic review and meta-analysis performed to synthesise the empirical evidence related to the use of inertial sensors for fall risk

assessment and prediction, in order to identify the optimal combination of sensor placement, movement task and measured variables or features.

The evidence collected in this study produced a comprehensive inventory of the sensor-based features that have been used for assessing the risk of falling in older adults and reported in the literature, including the difference between groups (non-fallers and fallers) and the statistical significance of these differences.

The statistical analysis of features above demonstrated that the combination 'angular velocity-walking-shins' has more discriminative power between non-fallers and fallers than other combinations. Moreover, the meta-analysis demonstrated that four features are significantly different between non-fallers and fallers. However, most features were not included in the meta-analysis because they were not reported with sufficient homogeneity in at least two studies, suggesting that future studies are required to produce more evidence that allows conducting a more comprehensive meta-analysis.

Overall, the results of this study suggest that the instrumented TUG test is a suitable tool for discriminating non-fallers and fallers, provided that the inertial sensors are placed on the shins and angular velocity, temporal (e.g. total time and step time) and spatial (e.g. number of steps) features are computed. These findings should contribute to closing the gap between research studies and clinical applications, by enabling the evidence-based design of new studies and real-life applications.

Nevertheless, these results are based on data extracted from a limited number of studies. Hence, there might be some other sensor-based features that are discriminant between non-fallers and fallers but were not included in this systematic review as they were not reported as required by the inclusion criteria.

This study led to the identification of an optimal inertial sensor-based protocol for fall risk assessment in older adults, thus answering the first research question underlying this thesis (see chapter 1). The study presented in the next chapter investigates whether quantitative descriptors of nonlinear system dynamics are more sensitive than linear measures to differences in balance control due to ageing and fall risk, thus addressing the second research question.

Chapter 4

Approximate Entropy and Sample Entropy for Fall Risk Assessment in Older Adults

4.1 Chapter overview

The diffusion of nonlinear dynamical systems theory into the biomedical research community has inspired the use of quantitative descriptors of nonlinear dynamics for assessing balance control. In particular, Approximate Entropy (ApEn) and Sample Entropy (SampEn) have been proposed as measures of body sway regularity during unperturbed standing. However, their ability to discriminate between groups with different fall risk and the suitable selection of the input parameters needed for their computation, have not yet been formally investigated. This chapter presents a study performed to investigate whether ApEn and SampEn are more sensitive than linear measures to differences in balance control due to ageing and fall risk, as well as to identify the optimal way to apply them (e.g. signal pre-processing, selection of input parameters, etc.).

4.2 Introduction

Centre of Pressure (CoP) time-series have been mostly characterised using linear measures, which describe the magnitude of CoP excursions in the time and frequency domains (e.g. path length and mean frequency of CoP motion, respectively). Age-related differences in these measures have been widely recognised, with older adults ($\geq$60 years old) showing generally larger CoP sways than young adults (18–59 years

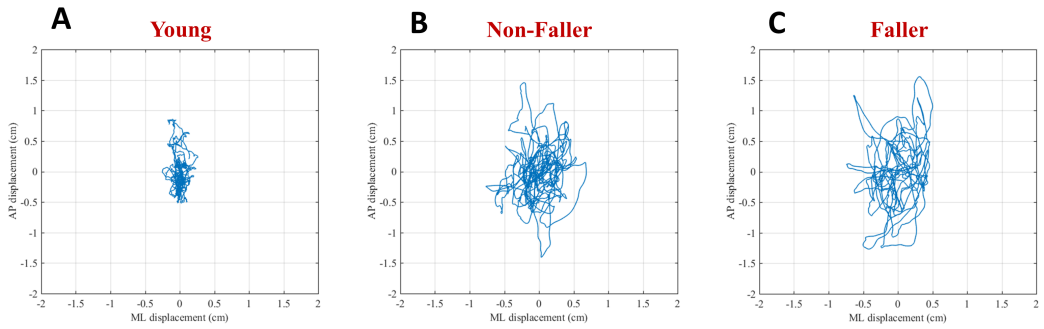

Figure 4.1: Representative centre of pressure (CoP) trajectories for **(A)** a young adult (27 years), **(B)** a non-faller (68 years) and **(C)** a faller (61 years). Older adults show generally wider CoP displacements than young adults. In contrast, CoP excursions from older adults with different fall risk are similar in terms of amplitude, making global measures inadequate to discriminate between them. Data sourced from the public dataset used in this study [27].

old) [2]. These differences are evident even through the visual inspection of CoP traces, as can be seen in Figure 4.1 panels A and B. In contrast, CoP excursions from older adults with different fall risk are similar in terms of amplitude, as can be seen in Figure 4.1 panels B and C.

Structural measures are sensitive to the structural variation in the time-series, thus they represent a potential alternative for describing differences in CoP excursions of a different nature. Entropy measures have been used for assessing the regularity of CoP time-series in different testing conditions and experimental groups [21, 95–109]. For instance, Cavanaugh *et al.* used ApEn to evaluate the effect of performing a secondary cognitive task on postural control in a sample of healthy young adults (n=30), as compared to performing a single task (i.e., posture control plus cognitive task versus posture control only) [97]. The authors observed generally higher ApEn values in the anterior-posterior CoP time-series during a dual task than during a single task. However, no significant differences in ApEn values for the medial-lateral direction were observed. In another study, Borg and Laxåback investigated the differences in SampEn values between young adults (n=45) and older adults (n=91) [21]. Significant differences between groups were observed for the Anterior-Posterior (AP) axis with higher values for older adults than for young adults. However, the ability of ApEn and SampEn to discriminate between groups of older adults with different risks of falling has not been investigated (e.g. non-fallers versus fallers).

A detailed definition of ApEn and SampEn is presented in section 2.4. Briefly,

given a time-series of length N, $ApEn(m, r, N)$ is the difference between the frequency that all the m-point subseries in the time-series are close to each other (within a tolerance given by $\pm r$ times the standard deviation of the time-series) and the frequency that all the $m + 1$-point subseries in the time-series are close to each other (again, within a tolerance given by $\pm r$ times the standard deviation of the time-series). Importantly, the ApEn algorithm counts each subseries as matching itself. As a consequence, the ApEn algorithm inherently produces a bias towards regularity. In order to counteract this shortcoming, the SampEn algorithm does not count self-matches. $SampEn(m, r, N)$ is the negative natural logarithm of the conditional probability that two subseries similar for m points remain similar for $m + 1$ points, where self-matches are not included in calculating the probability. In addition to eliminating self-matches, it has been shown that SampEn is mostly independent of the data length and shows more consistent behaviours than ApEn [111].

The appropriate selection of parameters m (subseries length), r (similarity tolerance) and N (data length) is critical. Traditionally, for clinical data, m is to be set at 2 or 3, r is to be set between 0.1 and 0.25 times the standard deviation of the data and N as equal to or greater than 1000 [110, 111]. However, these recommendations were based on the analysis of cardiac and respiratory time-series, thus do not always produce optimal results for all types of data. Therefore, an investigation of the effects of changing parameter values on the computation of ApEn and SampEn for specific types of data is needed. Nevertheless, the issue has not been investigated systematically when dealing with CoP time-series.

This chapter presents an original study performed: (1) to determine the ability of ApEn and SampEn to discriminate between experimental groups, especially between non-fallers and fallers; and, (2) to examine the effect of changing the value of the parameters m, r and N on ApEn and SampEn values in CoP time-series (e.g. signal pre-processing and selection of input parameters). The contents of this chapter have been published elsewhere [153].

ApEn and SampEn were selected among other nonlinear measures given that they are well suited to the analysis of short and noisy data. As mentioned above, these methods quantify the regularity or self-similarity of time-series by examining them for similar epochs or subseries: more frequent, similar subseries lead to lower entropy values. Thus low ApEn and SampEn values reflect a high degree of regularity or self-similarity [110, 111]. Regarding CoP time-series analysis, relatively high entropy values may be indicative of a balance control mechanisms that are too random to command balance properly, whereas relatively low values may describe a

balance control that is too stiff to cope with situations that require flexibility [21].

This study was motivated by the promising results obtained in a preliminary study, in which the issue of the adequate selection of ApEn and SampEn parameter values for CoP time-series analysis was partially addressed [154]. However, the present study represents a more comprehensive investigation of this issue, as it covers a broader range of parameter values, included the Medial-Lateral (ML) direction in addition to the AP direction and compared the ability of ApEn and SampEn to discriminate between experimental groups to that of traditional measures of CoP displacement. Therefore, the methods and results in the present study should be considered more robust and informative for future studies.

4.3 Methods

4.3.1 Dataset description

This study made use of an open dataset of human balance evaluations [27]. The dataset contains static posturography data from 163 participants. A detailed description of this protocol, the data pre-processing methods and the resulting dataset can be found elsewhere [155]. Briefly, CoP time-series were recorded while subjects were standing still for 60 seconds in four different conditions: with eyes open on a rigid surface, with eyes open on a foam mat, with eyes closed on a rigid surface, and with eyes closed on a foam mat. Three trials per condition were recorded, producing 1,930 trials in total (the authors reported 26 trials from 5 subjects as missing due to the inability of those subjects to complete the tasks). During the trials, 3D ground reaction forces and moments were recorded using a force platform with a sampling frequency of 100 Hz and were later used to compute the CoP position in the AP and ML axes. Importantly, the authors reported having smoothed the signals using a fourth-order zero-lag Butterworth low-pass filter with a cut-off frequency of 10 Hz. Previous studies have investigated the effects of digital filtering (specifically using a second-order dual-pass Butterworth low-pass filter) on linear and entropy measures of CoP displacement (Standard Deviation (SD)/Root Mean Square (RMS) value and sample entropy, respectively) [156, 157]. While digital filtering did not affect traditional measures [156], a decrease in sample entropy was reported for filtered data compared to unfiltered data [156, 157]. Therefore, should the present data analysis be replicated on unfiltered CoP data, higher entropy values would be expected to come out from it. Figure 4.2 shows representative CoP time-series taken from this dataset.

Additionally, the dataset contains sociodemographic, anthropometric, and

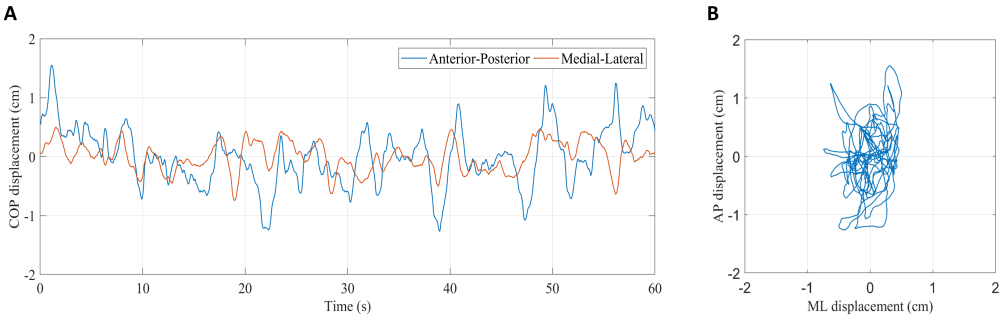

Figure 4.2: Representative centre of pressure time-series (CoP) for an older adult (61 years old) who experienced a fall within the past 12 months: **(A)** anterior-posterior (AP) and medial-lateral (ML) time-series versus time, and **(B)** medial-lateral versus anterior-posterior. Data sourced from the public dataset used in this study [27].

health status data for each participant (e.g. age, height, weight, morbidities and disabilities), as well as their history of falls (i.e.number of non-intentional falls in the past 12 months) and scores for other evaluations related to balance, fear of falling, physical activity and cognitive function. Age and history of falls were used to label subjects as Young, Non-Fallers and Fallers as described in subsection 4.3.3. Reported disabilities were used to discard subjects with physical disabilities from the data analysis.

This open dataset was collected by researchers from the Laboratory of Biomechanics and Motor Control at the Federal University of ABC (São Bernardo do Campo, Brazil) following a research protocol approved by the local ethics committee of the University (#842529/2014) [155].

4.3.2 Data processing

Besides m, r and N, the ApEn and SampEn algorithms allow adjusting a fourth parameter known as the time delay (τ) in the computation of entropy values. Generally speaking, by adjusting the time delay to a specific value of τ, the time-series used for the computation of ApEn/SampEn would be made of the first sample and then every τ^{th} sample after the first. In more formal terms, for a time-series X of length N, $X = \{x(1), x(2), x(3), \ldots, x(N)\}$, the computation of ApEn/SampEn with a time delay of τ would be performed on the time-series given by $X' = \{x(1), x(1+\tau), x(1+2\tau), \ldots, X(N-\tau+1)\}$. In a previous study, Kaffashi *et al.* [158] showed that, for time-series generated by non-linear dynamics that have a long-range autocorrelation (e.g. a slowly decaying Autocorrelation Function (ACF), such as those observed for CoP time-series), using a unity delay ($\tau = 1$)

would solely measure the linear autocorrelation properties of the signal. This would mask the ability of the ApEn/SampEn approach to quantify the regularity in the time-series resulting from long-range non-linear features. Therefore, the choice of the value of τ is crucial. For this type of data, using a higher time-delay value has been suggested [158]. Ideally, the choice of time delay must correspond to either the first minimum or zero-crossing of the ACF. However, an exploratory analysis of the CoP data used in this study revealed that these conditions were met for very large values of τ, which would leave a number of data points far below the minimum required to compute ApEn and SampEn. Therefore, τ was set to 5, as a compromise between data length and an acceptable reduction in ACF. This was implemented computationally by downsampling the CoP time-series by a factor of 5, indirectly adjusting the time delay ($\tau = 5$) in the computation of ApEn and SampEn [158]. Consequently, the downsampled data had an effective frequency of 20 Hz, resulting in a length of $N = 1200$ data points (20 Hz x 60 s).

To examine the effect of the choice of input parameters m, r and N, each CoP time-series was subjected to ApEn and SampEn calculation for all possible combinations of $m = 2, 3, 4, 5$, $r = 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5$ and $N = 600, 1200$ (i.e., 30 and 60 seconds, respectively). These ranges of input parameter values are more comprehensive than the ones adopted in previous studies, in which values of m equal to 2, 3 or 5 and r from 0.1 to 0.3 have been used [21, 95–98, 100–103, 107–109]. This choice was motivated by our interest in exploring the behaviour of ApEn and SampEn for a range of input parameters extending beyond the traditional values. A detailed description of the methods used to compute ApEn and SampEn was presented in section 2.4. As mentioned above, these methods quantify the regularity or self-similarity of time-series by examining them for similar epochs or subseries: more frequent, similar subseries led to lower entropy values. Thus low ApEn and SampEn values reflect a high degree of regularity or self-similarity [110, 111]. Regarding CoP time-series analysis, relatively high entropy values may be indicative of balance control mechanisms that are too random to command balance properly, whereas relatively low values may describe a balance control that is too stiff to cope with situations that require flexibility [21].

Additionally, CoP displacement linear measures were also computed as described in section 2.4: total length of displacement, the amplitude of displacement in the AP and ML axes, the standard deviation in the AP and ML axes, mean velocity in the AP and ML axes, total mean velocity and area covered by the displacement. These measures were computed for detrended CoP time-series (i.e. mean value subtracted) of length $N = 1200$, i.e. 60-second recordings (in line with the

latest recommendations [188]) at an effective frequency of 20 Hz (that is, twice the frequency of the CoP signal, in line with the Nyquist theorem).

A block diagram depicting the steps followed for data processing is shown in Figure 4.3. The scripts for data processing were written in MATLAB R2017b (The Mathworks, Inc., Natick, MA, USA). The source code can be found in Appendix A.

4.3.3 Data analysis

4.3.3.1 Effects of changing input parameters on approximate and sample entropy

A three-way Analysis of Variance (ANOVA) was conducted to determine the effect of changing m, r and N on ApEn and SampEn values. As described before, there were four levels of m (i.e., 2, 3, 4, 5), nine levels of r (i.e. 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5) and two levels of N (i.e. 600 and 1200). A significant three-way interaction between m, r, and N (p-value$<$0.05) indicated that entropy values changed significantly for one or more combinations of m, r and N. Otherwise, a significant two-way interaction indicated that entropy values changed significantly for one or more combinations of those two parameters, yet entropy values were not significantly different across the values for the third parameter. These analyses were performed including ApEn and SampEn values for all CoP time-series, regardless of testing condition (i.e. all trials per testing condition were included).

Additionally, the contributions of each factor (i.e. main factors m, r and N, and their interactions) to the variation of ApEn and SampEn values were quantified by the partial eta-squared measure, η_p^2, which is computed as follows:

$$\eta_p^2 = \frac{SumSq_{factor}}{SumSq_{factor} + SumSq_{error}} \tag{4.1}$$

where $SumSq_{factor}$ is the variation attributable to the factor and $SumSq_{error}$ is the error variation [159], as derived from the three-way ANOVA. The higher the η_p^2 value, the stronger the contribution of a factor is to the variation of ApEn and SampEn [159].

4.3.3.2 Ability of approximate and sample entropy to discriminate between non-fallers and fallers

Firstly, subjects were grouped based on their age and history of falls in the past 12 months: young adults (Young, age$<$60), older adults (age$\geq$60) without falls in the last 12 months (Non-Fallers) and older adults (age$\geq$60) who experienced one or

more falls in the last 12 months (Fallers). Subjects with reported physical disabilities were excluded from the analysis.

Subsequently, ApEn and SampEn group mean and standard deviation values by group for all combinations of m, r and N were computed, regardless of testing condition. To determine the effects of group on ApEn and SampEn, a mixed-design ANOVA was conducted. It consisted of one between-subjects factor (i.e., group) and three within-subjects factors (i.e., m, r and N). There were three levels of group (i.e. Young, Non-Fallers and Fallers); the levels for the within-subject factors have been introduced above. A significant four-way interaction between group, m, r and N indicated that the entropy values were different between at least two groups for one or more combinations of m, r and N. These combinations were identified by performing a *post hoc* analysis of the differences between groups for each combination of m, r and N using the Tukey's honest significant difference procedure. A p-value<0.05 was accepted as evidence of statistical significance.

In addition, the statistical significance of differences in linear measures between groups was also determined using a one-way ANOVA and a post hoc analysis (Tukey's honest significant difference procedure). These latter analyses were performed in order to compare the ability of ApEn and SampEn to discriminate between different groups to that of the more standard methods.

4.3.3.3 Behaviour of sample entropy in different testing conditions

Additionally, the behaviour of SampEn in different testing conditions was also investigated. Namely, SampEn mean and standard deviation values by group for all combinations of m, r and N were computed separately for each testing condition: Eyes open on a rigid surface (OR), Eyes closed on a rigid surface (CR), Eyes open on a foam mat (OF) and Eyes closed on a foam mat (CF). For each testing condition, a one-way ANOVA with group as a factor, as well as a *post hoc* analysis (Tukey's honest significant difference), was performed for each parameter combination. These analyses were carried out in order to determine whether a specific testing condition might boost the sensitivity of SampEn to differences between groups (e.g. more parameter combinations produced significant differences between groups). These analyses were performed only on SampEn values from CoP time-series in the anterior-posterior direction, as the analyses described earlier revealed that these were more sensitive to differences between groups, especially between Non-Fallers and Fallers.

All statistical analyses were performed in MATLAB R2017b.

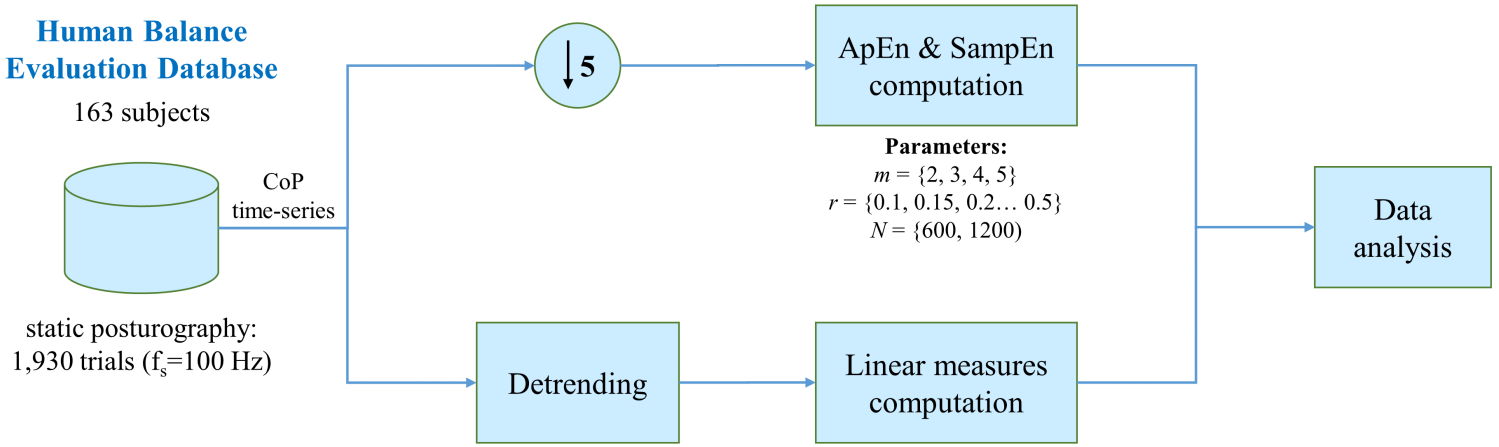

Figure 4.3: Block diagram of centre of pressure (CoP) data processing. Approximate and sample entropy were computed for 72 different combinations of input parameters after downsampling CoP time-series by a factor of 5. Linear measures were computed on detrended CoP time-series (i.e. mean value subtracted).

4.4 Results

4.4.1 Effects of changing input parameters on approximate and sample entropy

For ApEn in the anterior-posterior direction, the three-way ANOVA with m, r, and N as factors revealed statistically significant main effects of m, r and N. These main effects were qualified by an interaction between m, r and N (Table 4.1). For ApEn in the medial-lateral direction, the three-way ANOVA revealed statistically significant main effects of m, r and N. These main effects were qualified by an interaction between m, r and N (Table 4.1). The existence of significant three-way interactions suggests that ApEn values changed significantly for different combinations of m, r and N.

For SampEn in the anterior-posterior direction, a three-way ANOVA with m, r, and N as factors revealed a main effects of m, r and N. These main effects were qualified by interactions between m and r, between m and N and between r and N. The interaction between m, r, and N was not significant (Table 4.2). For SampEn in the medial-lateral direction, the three-way ANOVA revealed a main effects of m, r and N. These main effects were qualified by interactions between m and r, m and N, and r and N. The interaction between m, r, and N was not significant (Table 4.2). The existence of significant two-way interactions suggests that SampEn values changed significantly for one or more combinations of these two parameters, yet entropy values were not significantly different across the values for the third parameter.

These findings are illustrated in Figure 4.4, where ApEn and SampEn for the AP component are presented as a function of m, r and N. It can be observed that the shape of ApEn as a function of r was different for different combinations of m and N (top panels). As for SampEn, its values tended to decrease as r increased, yet its shape was consistent across different combinations of m and N (bottom panels). Interestingly, subplots c) and d) in Figure 4.4 suggest a reciprocal relationship between r and SampEn. ApEn and SampEn showed a similar behaviour for the ML component of the CoP time-series (see Figure S1 in Appendix C).

Table 4.1: Effects of input parameters on approximate entropy: three-way ANOVA summary table.

A) Anterior-posterior direction

Source	Sum Sq.	d.f.	Mean Sq.	F	p	η_p^2
m	209.58	3	69.862	8195.1	< 0.001	0.1504
r	1327.60	8	165.952	19467	< 0.001	0.5286
N	0.22	1	0.220	25.8	< 0.001	0.0002
$m * r$	193.92	24	8.080	947.8	< 0.001	0.1407
$m * N$	6.05	3	2.016	236.5	< 0.001	0.0051
$r * N$	25.22	8	3.152	369.7	< 0.001	0.0209
$m * r * N$	2.62	24	0.109	12.8	< 0.001	0.0022
Error	1184	138888	0.009			
Total	2949.20	138959				

B) Medial-lateral direction

Source	Sum Sq.	d.f.	Mean Sq.	F	p	η_p^2
m	224.69	3	74.896	13287	< 0.001	0.223
r	1284.3	8	160.537	28481	< 0.001	0.6213
N	1.04	1	1.036	183.78	< 0.001	0.0013
$m * r$	175.31	24	7.305	1295.9	< 0.001	0.183
$m * N$	6.28	3	2.092	371.18	< 0.001	0.008
$r * N$	22.98	8	2.873	509.64	< 0.001	0.0285
$m * r * N$	2.02	24	0.084	14.9	< 0.001	0.0026
Error	782.87	138888	0.006			
Total	2499.5	138959				

Sum Sq. type III sum of squares, *d.f.* degrees of freedom, *Mean Sq.* mean square, F F-statistic, p p-value, η_p^2 partial eta-squared

Table 4.2: Effects of input parameters on sample entropy - three-way ANOVA summary table

A) Anterior-posterior direction

Source	Sum Sq.	d.f.	Mean Sq.	F	p	η_p^2
m	43.13	3	14.3753	1195.4	< 0.001	0.0252
r	2463.90	8	307.9882	25612	< 0.001	0.5960
N	17.04	1	17.0362	1416.7	< 0.001	0.0101
$m * r$	20.04	24	0.8351	69.4	< 0.001	0.0119
$m * N$	0.71	3	0.2357	19.6	< 0.001	0.0004
$r * N$	0.36	8	0.0455	3.8	< 0.001	0.0002
$m * r * N$	0.08	24	0.0034	0.3	1	0
Error	1670.2	138888	0.012			
Total	4215.4	138959				

B) Medial-lateral direction

Source	Sum Sq.	d.f.	Mean Sq.	F	p	η_p^2
m	59.34	3	19.7808	2561.1	< 0.001	0.0524
r	2199.40	8	274.9212	35595.0	< 0.001	0.6722
N	21.01	1	21.0063	2719.8	< 0.001	0.0192
$m * r$	28.42	24	1.1841	153.3	< 0.001	0.0258
$m * N$	0.94	3	0.3133	40.6	< 0.001	0.0009
$r * N$	0.42	8	0.0521	6.7	< 0.001	0.0004
$m * r * N$	0.10	24	0.0041	0.5	0.969	0.0001
Error	1072.70	138888	0.0077			
Total	3382.30	138959				

Sum Sq. type III sum of squares, *d.f.* degrees of freedom, *Mean Sq.* mean square, F F-statistic, p p-value, η_p^2 partial eta-squared

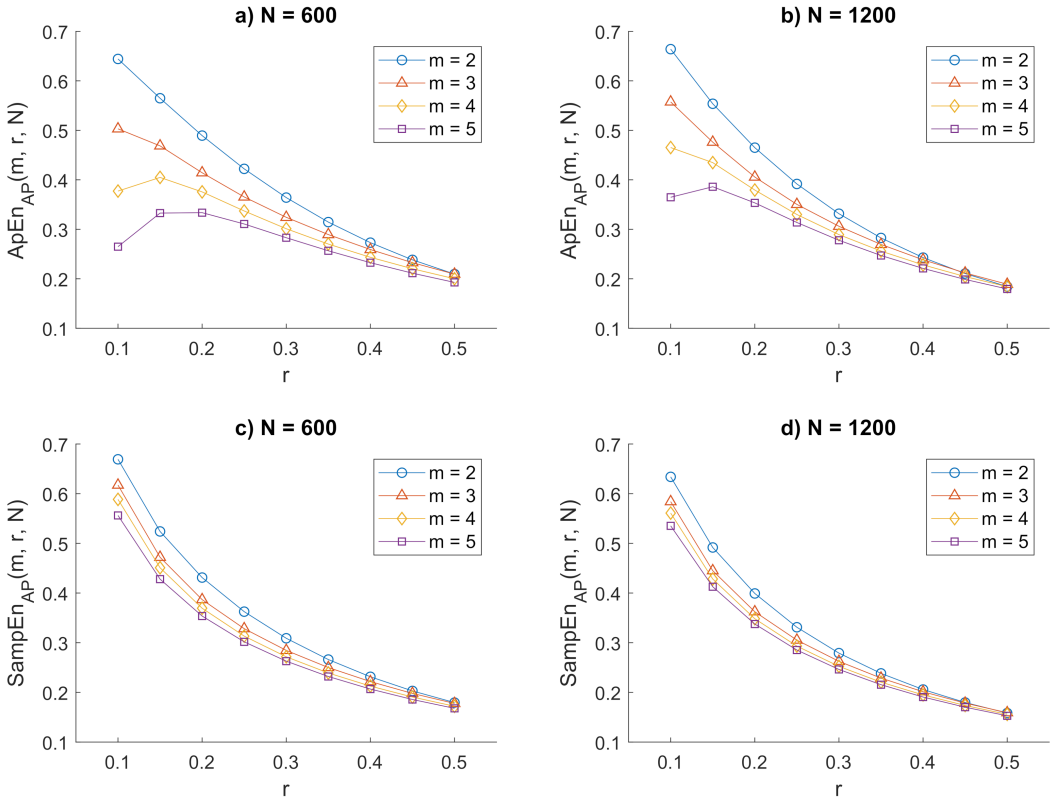

Figure 4.4: Approximate entropy (ApEn) and sample entropy (SampEn) as a function of m, r and N for the anterior-posterior (AP) component of the centre of pressure displacement during unperturbed standing: **a)** ApEn for $N = 600$, **b)** ApEn for $N = 1200$, **c)** SampEn for $N = 600$, and **d)** SampEn for $N = 1200$

4.4.2 Ability of approximate and sample entropy to discriminate between non-fallers and fallers

4.4.2.1 Participant grouping and characteristics

The CoP data from four participants were discarded from this analysis due to physical disabilities (namely, poliomyelitis and cerebral palsy), leaving 159 participants (115 females, 44 males) for the analysis: 85 subjects were young adults (Young), 56 subjects were older adults without falls in the last 12 months (Non-Fallers), and 18 subjects were older adults with one or more falls in the last 12 months (Fallers). Table 4.3 shows the mean value (standard deviation) for participant characteristics by group: age, height, weight and Body Mass Index (BMI). Moreover, it shows results from a one-way ANOVA and *post hoc* comparisons between groups carried out using the Tukey's honest significant difference procedure. No significant differences were observed between the Non-Fallers and Fallers groups, suggesting homogeneity between them concerning age and anthropometric variables (thus discarding those characteristics as potential confounders).

4.4.2.2 Approximate entropy

A significant four-way interaction between group, m, r and N was found [Anterior-Posterior: $F(6.96, 6601) = 16.3$, $p < 0.001$, $\eta_p^2 = 0.17$; Medial-Lateral: $F(6.99, 6624) = 5.43$, $p < 0.001$, $\eta_p^2 = 0.006$]. This indicated that the ApEn values were different between at least two groups for one or more combinations of m, r and N. Importantly, the p-values reported above were produced by applying the Greenhouse-Geisser procedure, since the data violated the assumption of sphericity imposed by the mixed-ANOVA test (i.e. Mauchly's test with a $p < 0.001$ for both anterior-posterior and medial-lateral CoP). The term *sphericity* refers to the condition where the variances in the differences between all possible pairs of factors (i.e. group, m, r and N) are equal. If this assumption is violated, then the mixed-ANOVA test results in an inflated F-statistic and thus deflated p-values. The Greenhouse-Geisser correction adjusts the degrees of freedom in the mixed-ANOVA so that a valid F-statistic can be obtained [160].Therefore, the reported p-values represent a more conservative approach and thus the results can be considered more valid.

Young versus Older adults (Non-Fallers and Fallers). For $N = 1200$ (i.e. 60 seconds) in the AP direction, Fallers and Non-Fallers showed generally higher ApEn mean values than Young adults (Figure 4.5). There was only one exception to this trend (namely, for $ApEn(m = 5, r = 0.1)$) for which Fallers had a slightly lower

ApEn mean value than Young adults (a behaviour hereon referred to as "trend flip" or "crossover"). Statistical testing revealed that those differences were significant ($p < 0.05$) for all combinations of m and r (Table 4.4). In the ML direction, Fallers had lower ApEn mean values than Young adults for all combinations of m and r (see Figure S2 in Appendix C). However, statistical testing revealed that only one combination of m and r produced significant differences between groups (see Table S2 in Appendix C). The differences between Young adults and Non-Fallers did not exhibit a consistent trend.

For $N = 600$ (i.e. 30 seconds), in the AP direction, similar trends to those for longer data lengths ($N = 1200$) were observed. Namely, older adults showed generally higher ApEn mean values than young adults, with a decreased consistency in trend (3 trend flips for $N = 600$ versus one trend flip for $N = 1200$) (see Figure S3 in Appendix C). These differences were statistically significant ($p < 0.05$) for all but one combination of m and r (see Table S3 in Appendix C). In the ML direction, Fallers generally showed lower ApEn mean values than Young adults, in partial agreement with the results obtained for $N = 1200$ (see Figure S4 in Appendix C). The dissimilarities observed were that, in contrast to the trend observed for $N = 1200$, the trend observed for $N = 600$ was not consistent for all combinations of m and r (i.e. some flips appeared for shorter data length) and was found to be statistically significant for some combinations of m and r (see Table S4 in Appendix C). As for the differences between Non-Fallers and Young adults, no consistent trend was observed, in agreement with the results for a data length of $N = 1200$.

Older adults, Non-Faller versus Fallers. For $N = 1200$ (i.e. 60 seconds) in the AP direction, Fallers showed generally higher ApEn mean values than Non-Fallers (Figure 4.5). Some exceptions to this trend were found: $ApEn(m = 4, r = 0.1)$ and $ApEn(m = 5, r = \{0.1, 0.15\})$. However, statistical testing revealed significant differences only for specific parameter combinations (Table 4.4). In the ML direction, Fallers exhibited lower ApEn mean values than Non-Fallers for all combinations of m and r (see Figure S2 in Appendix C). However, statistical testing revealed that only two combinations of m and r produced significant differences between groups (see Table S2 in Appendix C).

Table 4.3: Participant characteristics by group. There are no significant differences between the Non-Fallers and Fallers groups, suggesting homogeneity between them concerning age and anthropometric variables (thus discarding those characteristics as potential confounders

	One-way ANOVA		Descriptive statistics by group			Post hoc					
			Young (Y) (n=85)	Non-Fallers (NF) (n=56)	Fallers (F) (n=18)	NF - Y		F - Y		F - NF	
Variable	F	p-value	Mean (SD)	Mean (SD)	Mean (SD)	MD	p-value	MD	p-value	MD	p-value
Age, years	722.3	**<0.001**	27.7 (7.78)	71.5 (6.35)	71.2 (7.12)	43.8	**<0.001**	43.5	**<0.001**	-0.3	0.984
Height, cm	26.2	**<0.001**	166.8 (8.75)	157.8 (8.73)	155.2 (6.16)	-9	**<0.001**	-11.6	**<0.001**	-2.6	0.502
Weight, kg	2.24	0.110	61.6 (7.73)	63.9 (8.43)	60 (8.10)	2.3	0.207	-1.6	0.718	-3.9	0.163
BMI, kg/m^2	26.7	**<0.001**	22.2 (2.82)	25.7 (2.97)	24.9 (2.84)	3.5	**<0.001**	2.7	**0.001**	-0.8	0.540

F F-statistic, *SD* standard deviation, *MD* mean difference, *BMI* body mass index
Bold values indicate significant differences

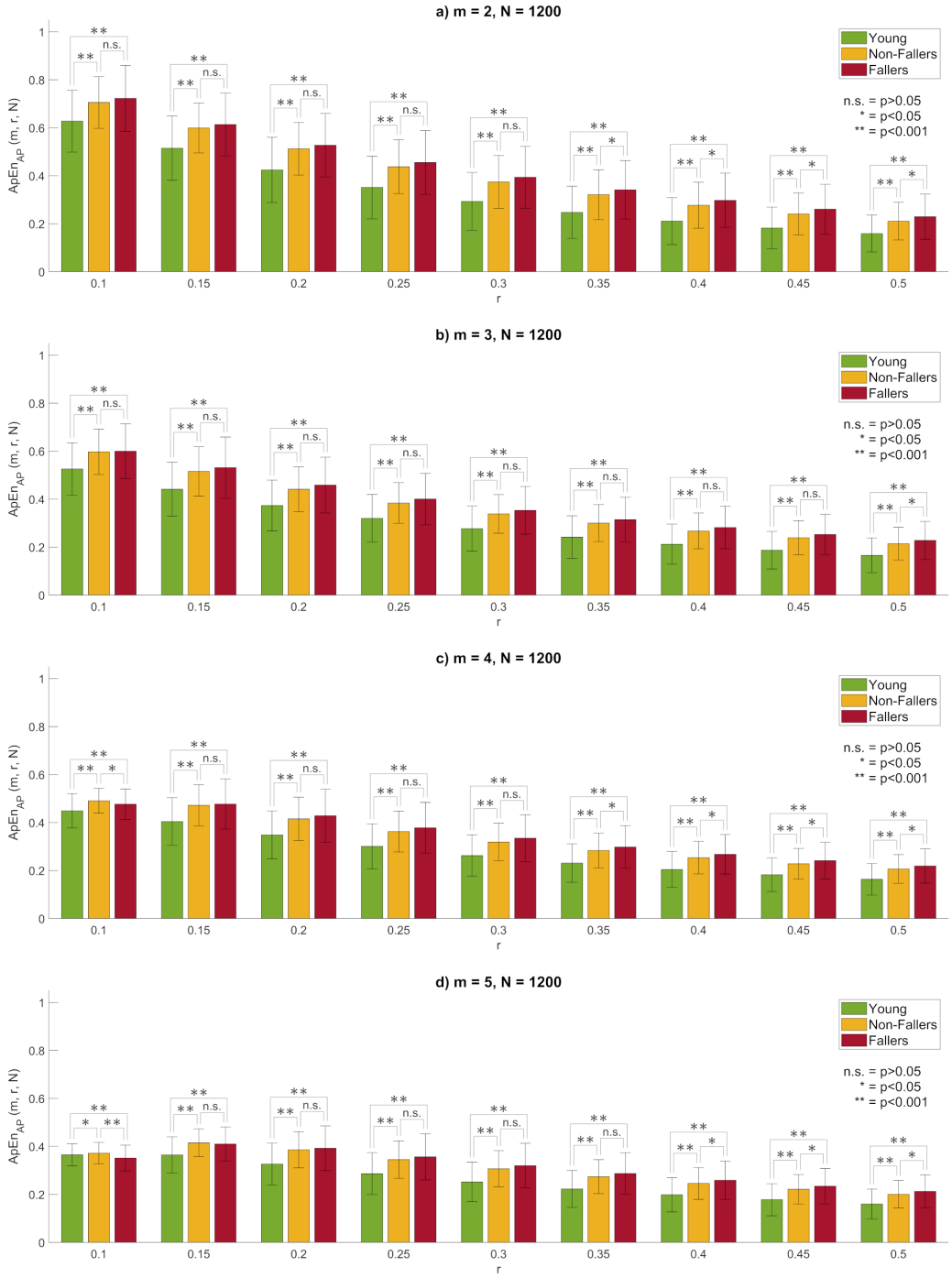

Figure 4.5: Approximate entropy (ApEn) mean value (bars) and standard deviation (error lines) by group as a function of r for $m = 2, 3, 4, 5$ and $N = 1200$ (i.e. 60 seconds) for the anterior-posterior (AP) component of the centre of pressure displacement during unperturbed standing: **a)** $m = 2$, **b)** $m = 3$, **c)** $m = 4$, and **d)** $m = 5$

Table 4.4: Approximate entropy in the anterior-posterior direction as a function of r and m for a data length of $N = 1200$ (i.e. 60-seconds).

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	F	p-value	Mean	SD	Mean	SD	Mean	SD	MD	p-value	MD	p-value	MD	p-value
m = 2														
0.1	105.45	**<0.001**	0.628	0.129	0.705	0.108	0.723	0.138	0.078	**<0.001**	0.095	**<0.001**	0.017	0.178
0.15	119.31	**<0.001**	0.515	0.134	0.599	0.104	0.613	0.131	0.084	**<0.001**	0.099	**<0.001**	0.015	0.298
0.2	124.58	**<0.001**	0.424	0.136	0.512	0.110	0.527	0.133	0.088	**<0.001**	0.103	**<0.001**	0.015	0.28
0.25	126.90	**<0.001**	0.351	0.131	0.438	0.113	0.455	0.133	0.087	**<0.001**	0.104	**<0.001**	0.018	0.176
0.3	126.80	**<0.001**	0.293	0.121	0.374	0.110	0.394	0.129	0.081	**<0.001**	0.101	**<0.001**	0.019	0.093
0.35	125.88	**<0.001**	0.247	0.109	0.321	0.104	0.341	0.122	0.074	**<0.001**	0.094	**<0.001**	0.020	**0.049**
0.4	124.51	**<0.001**	0.211	0.098	0.277	0.096	0.297	0.113	0.066	**<0.001**	0.086	**<0.001**	0.020	**0.024**
0.45	123.46	**<0.001**	0.182	0.087	0.241	0.087	0.260	0.104	0.059	**<0.001**	0.078	**<0.001**	0.020	**0.014**
0.5	122.47	**<0.001**	0.159	0.077	0.211	0.079	0.229	0.094	0.052	**<0.001**	0.070	**<0.001**	0.019	**0.009**
m = 3														
0.1	111.29	**<0.001**	0.526	0.109	0.597	0.094	0.600	0.114	0.071	**<0.001**	0.074	**<0.001**	0.003	0.939
0.15	118.46	**<0.001**	0.441	0.113	0.516	0.103	0.531	0.128	0.074	**<0.001**	0.090	**<0.001**	0.016	0.170
0.2	117.94	**<0.001**	0.374	0.106	0.441	0.093	0.459	0.117	0.068	**<0.001**	0.085	**<0.001**	0.017	0.080
0.25	121.98	**<0.001**	0.32	0.099	0.384	0.085	0.400	0.107	0.064	**<0.001**	0.080	**<0.001**	0.016	0.073
0.3	123.27	**<0.001**	0.277	0.094	0.338	0.081	0.353	0.099	0.061	**<0.001**	0.076	**<0.001**	0.015	0.088
0.35	125.37	**<0.001**	0.242	0.089	0.300	0.078	0.314	0.094	0.058	**<0.001**	0.073	**<0.001**	0.014	0.084
0.4	125.87	**<0.001**	0.212	0.084	0.267	0.075	0.282	0.089	0.055	**<0.001**	0.070	**<0.001**	0.014	0.064
0.45	125.41	**<0.001**	0.187	0.078	0.239	0.072	0.253	0.084	0.052	**<0.001**	0.066	**<0.001**	0.014	0.057
0.5	124.92	**<0.001**	0.166	0.073	0.214	0.068	0.228	0.079	0.048	**<0.001**	0.062	**<0.001**	0.014	**0.043**

Table 4.4 continued from previous page

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	F	p-value	Mean	SD	Mean	SD	Mean	SD	MD	p-value	MD	p-value	MD	p-value
m = 4														
0.1	88.78	**<0.001**	0.449	0.072	0.491	0.052	0.477	0.064	0.042	**<0.001**	0.028	**<0.001**	-0.014	0.013
0.15	124.48	**<0.001**	0.404	0.099	0.472	0.086	0.477	0.105	0.068	**<0.001**	0.073	**<0.001**	0.005	0.785
0.2	121.79	**<0.001**	0.348	0.100	0.415	0.091	0.428	0.111	0.067	**<0.001**	0.080	**<0.001**	0.013	0.203
0.25	121.37	**<0.001**	0.301	0.094	0.362	0.085	0.378	0.106	0.062	**<0.001**	0.077	**<0.001**	0.016	0.075
0.3	121.01	**<0.001**	0.262	0.087	0.319	0.078	0.334	0.097	0.057	**<0.001**	0.072	**<0.001**	0.015	0.054
0.35	122.14	**<0.001**	0.231	0.080	0.283	0.073	0.298	0.089	0.052	**<0.001**	0.067	**<0.001**	0.015	**0.045**
0.4	123.08	**<0.001**	0.205	0.075	0.254	0.068	0.268	0.082	0.049	**<0.001**	0.063	**<0.001**	0.014	**0.041**
0.45	122.91	**<0.001**	0.182	0.070	0.228	0.064	0.241	0.076	0.046	**<0.001**	0.059	**<0.001**	0.013	**0.041**
0.5	123.17	**<0.001**	0.163	0.066	0.206	0.060	0.219	0.071	0.043	**<0.001**	0.055	**<0.001**	0.013	**0.036**
m = 5														
0.1	15.41	**<0.001**	0.365	0.046	0.372	0.045	0.352	0.054	0.007	**0.009**	-0.013	**<0.001**	-0.020	**<0.001**
0.15	119.49	**<0.001**	0.364	0.076	0.415	0.058	0.410	0.071	0.051	**<0.001**	0.046	**<0.001**	-0.005	0.634
0.2	126.02	**<0.001**	0.326	0.088	0.386	0.076	0.393	0.093	0.060	**<0.001**	0.066	**<0.001**	0.006	0.604
0.25	1240	**<0.001**	0.286	0.087	0.345	0.078	0.357	0.096	0.059	**<0.001**	0.070	**<0.001**	0.012	0.192
0.3	122.77	**<0.001**	0.252	0.083	0.307	0.075	0.32	0.093	0.055	**<0.001**	0.068	**<0.001**	0.013	0.097
0.35	122.05	**<0.001**	0.223	0.077	0.274	0.071	0.287	0.086	0.051	**<0.001**	0.064	**<0.001**	0.014	0.061
0.4	122.10	**<0.001**	0.198	0.072	0.246	0.066	0.259	0.080	0.047	**<0.001**	0.060	**<0.001**	0.013	**0.045**
0.45	121.42	**<0.001**	0.178	0.067	0.221	0.062	0.234	0.074	0.044	**<0.001**	0.056	**<0.001**	0.013	**0.036**
0.5	121.54	**<0.001**	0.160	0.062	0.200	0.058	0.213	0.069	0.041	**<0.001**	0.053	**<0.001**	0.012	**0.029**

F F-statistic, *SD* standard deviation, *MD* mean difference

Bold values indicate significant differences

For $N = 600$ (i.e. 30 seconds) in the AP direction, the relative consistency of ApEn and its ability to discriminate between Non-Fallers and Fallers were challenged. Firstly, more trend flips were observed for shorter time-series ($N = 600$) than for longer ones ($N = 1200$) (see Figure S3 in Appendix C). Also, statistical significance was only observed for combinations of m and r producing trend flips, thus casting doubt on its legitimacy (see Table S3 in Appendix C). In the ML direction, similar trends in group differences were observed for shorter data lengths ($N = 600$) compared to longer data length ($N = 1200$). Namely, Fallers showed generally lower ApEn mean values than Non-Fallers, with a slightly less consistent trend (1 trend flips for $N = 600$ versus any flip for $N = 1200$) (see Figure S4 in Appendix C). Moreover, in agreement with results for $N = 1200$, only specific combinations of m and r produced statistically significant trends (see Table S4 in Appendix C).

4.4.2.3 Sample entropy

A significant four-way interaction between group, m, r and N was found [Anterior-Posterior: $F(4.82, 4571 = 6.71$, $p < 0.001$, partial $\eta^2 = 0.007$; Medial-Lateral: $F(6.7, 6354) = 2.18$, $p = 0.035$, partial $\eta^2 = 0.002$]. This indicated that the SampEn values were different between at least two groups for one or more combinations of m, r and N. Once again, the reported p-values are the corrected ones using the Greenhouse-Geisser procedure, given that the compound symmetry assumption was violated (Mauchly's test with a $p < 0.001$ for both anterior-posterior and medial-lateral CoP time-series).

Young versus Older adults (Non-Fallers and Fallers). For $N = 1200$ (i.e. 60 seconds) in the AP direction, Fallers and Non-Fallers showed higher SampEn mean values than Young adults for all combinations of m and r (Figure 4.6). Those differences were found statistically significant with a $p < 0.001$ (Table 3). In the ML direction, Non-Fallers had higher SampEn mean values than Young adults for all combinations of m and r (see Figure S5 in Appendix C). In contrast, Fallers generally had lower values compared to Young adults. However, all those differences between Young and Non-Fallers/Fallers were found not statistically significant (see Table S5 in Appendix C).

For $N = 600$ (i.e. 30 seconds) in the AP direction, the relative trend consistency of SampEn and its ability to discriminate between Young adults and older adults (both Fallers and Non-Fallers) were preserved. Namely, Non-Fallers and Fallers showed higher SampEn mean values than Young adults for all combinations of m and r (see Figure S6 in Appendix C). Those differences remained statistically sig-

nificant with $p-value < 0.001$ (Table S6 in Appendix C). In the ML direction, some combinations of m and r produced statistically significant differences between Young adults and Fallers (see Table S7 in Appendix C), an unexpected result considering that no significant differences between groups were observed for longer time-series ($N = 1200$). More specifically, Fallers showed lower SampEn mean values than Young adults (Figure S7 in Appendix C). On the other hand, the relative trend consistency in differences between Young adults and Non-Fallers was challenged, corrupting the consistent trend observed for longer time-series ($N = 1200$) for which Non-Fallers showed higher SampEn values than Young adults for all combinations of m and r.

Older adults, Non-Faller versus Fallers. For $N = 1200$ (i.e. 60 seconds) in the AP direction, Fallers exhibited higher SampEn mean values than Non-Fallers for all combinations of m and r (Figure 4.6). However, statistical testing revealed significant differences only for specific parameter combinations (Table 3). In the ML direction, Fallers exhibited lower SampEn mean values than Non-Fallers for all combinations of m and r (see Figure S5 in Appendix C). No significant differences were found between Non-Fallers and Fallers (Table S5 in Appendix C).

For $N = 600$ (i.e. 30 seconds) in the AP direction, the ability of SampEn to discriminate between Non-Fallers and Fallers was challenged. Namely, no statistically significant differences between Non-Fallers and Fallers were observed (Table S6 in Appendix C), even if a consistent decrease was preserved (Figure S6 in Appendix C). In the ML direction, two combinations of m and r produced statistically significant differences between Non-Fallers and Fallers (Table S7 in Appendix C), with Fallers showing lower SampEn mean values than Non-Fallers (Figure S7 in Appendix C). These results differ from the results obtained with longer CoP time-series ($N = 1200$), where no significant differences were observed.

4.4.2.4 Linear measures

Both Fallers and Non-Fallers exhibited higher mean values than Young adults for all linear measures of CoP displacement. These differences were found statistically significant with a $p < 0.001$. Moreover, Fallers exhibited higher mean values than Non-Fallers for all linear measures. However, those differences did not reach statistical significance (Table 4.6).

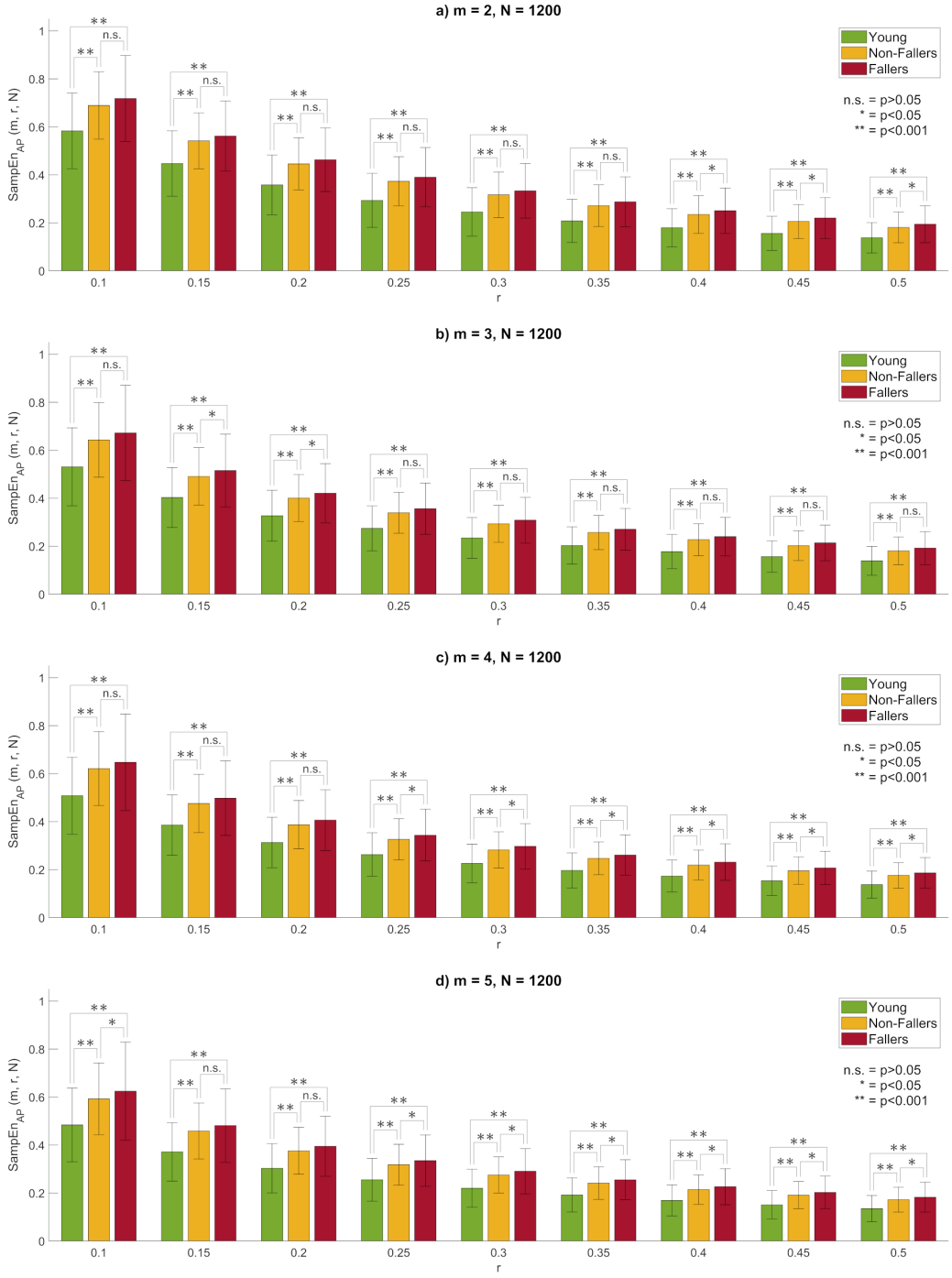

Figure 4.6: Sample entropy (SampEn) mean value (bars) and standard deviation (error lines) by group as a function of r for $m = 2, 3, 4, 5$ and $N = 1200$ (i.e. 60 seconds) for the AP component of the CoP displacement during unperturbed standing: **a)** $m = 2$, **b)** $m = 3$, **c)** $m = 4$, and **d)** $m = 5$

Table 4.5: Sample entropy in the anterior-posterior direction as a function of r and m for a data length of $N = 1200$ (i.e. 60-seconds)

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	F	p-value	Mean	SD	Mean	SD	Mean	SD	MD	p-value	MD	p-value	MD	p-value
m = 2														
0.1	128.20	**<0.001**	0.583	0.158	0.689	0.140	0.718	0.179	0.106	**<0.001**	0.134	**<0.001**	0.028	0.051
0.15	138.04	**<0.001**	0.447	0.136	0.542	0.116	0.562	0.146	0.094	**<0.001**	0.115	**<0.001**	0.020	0.125
0.2	139.12	**<0.001**	0.358	0.124	0.445	0.109	0.463	0.133	0.087	**<0.001**	0.105	**<0.001**	0.018	0.149
0.25	137.79	**<0.001**	0.294	0.113	0.373	0.102	0.390	0.123	0.080	**<0.001**	0.097	**<0.001**	0.017	0.116
0.3	134.96	**<0.001**	0.245	0.101	0.316	0.095	0.333	0.114	0.071	**<0.001**	0.088	**<0.001**	0.017	0.082
0.35	132.15	**<0.001**	0.208	0.090	0.271	0.087	0.288	0.104	0.063	**<0.001**	0.079	**<0.001**	0.016	0.058
0.4	129.41	**<0.001**	0.179	0.080	0.235	0.079	0.250	0.095	0.056	**<0.001**	0.071	**<0.001**	0.016	**0.040**
0.45	126.97	**<0.001**	0.156	0.071	0.205	0.071	0.220	0.085	0.049	**<0.001**	0.064	**<0.001**	0.015	**0.030**
0.5	125.08	**<0.001**	0.137	0.063	0.181	0.064	0.194	0.077	0.044	**<0.001**	0.057	**<0.001**	0.013	**0.025**
m = 3														
0.1	126.15	**<0.001**	0.531	0.163	0.643	0.156	0.672	0.199	0.112	**<0.001**	0.141	**<0.001**	0.029	0.064
0.15	132.96	**<0.001**	0.403	0.125	0.491	0.120	0.515	0.152	0.088	**<0.001**	0.113	**<0.001**	0.025	**0.037**
0.2	133.72	**<0.001**	0.327	0.106	0.401	0.098	0.421	0.124	0.074	**<0.001**	0.094	**<0.001**	0.020	**0.041**
0.25	135.48	**<0.001**	0.274	0.094	0.339	0.085	0.356	0.107	0.065	**<0.001**	0.082	**<0.001**	0.017	0.051
0.3	134.96	**<0.001**	0.234	0.085	0.294	0.077	0.308	0.096	0.059	**<0.001**	0.074	**<0.001**	0.015	0.069
0.35	134.70	**<0.001**	0.203	0.078	0.257	0.071	0.270	0.087	0.054	**<0.001**	0.067	**<0.001**	0.013	0.073
0.4	133.25	**<0.001**	0.178	0.071	0.227	0.066	0.240	0.080	0.050	**<0.001**	0.062	**<0.001**	0.012	0.066
0.45	131.57	**<0.001**	0.157	0.066	0.202	0.062	0.214	0.074	0.045	**<0.001**	0.057	**<0.001**	0.012	0.061
0.5	129.87	**<0.001**	0.139	0.06	0.181	0.058	0.192	0.069	0.042	**<0.001**	0.053	**<0.001**	0.011	0.053

Table 4.5 continued from previous page

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	F	p-value	Mean	SD	Mean	SD	Mean	SD	MD	p-value	MD	p-value	MD	p-value
m = 4														
0.1	128.60	**<0.001**	0.508	0.161	0.621	0.154	0.647	0.201	0.113	**<0.001**	0.140	**<0.001**	0.026	0.102
0.15	133.16	**<0.001**	0.386	0.126	0.476	0.122	0.498	0.155	0.090	**<0.001**	0.112	**<0.001**	0.022	0.072
0.2	132.77	**<0.001**	0.313	0.105	0.387	0.101	0.407	0.126	0.074	**<0.001**	0.094	**<0.001**	0.019	0.051
0.25	133.28	**<0.001**	0.263	0.091	0.326	0.086	0.344	0.108	0.064	**<0.001**	0.081	**<0.001**	0.018	**0.039**
0.3	132.67	**<0.001**	0.226	0.081	0.282	0.076	0.297	0.095	0.056	**<0.001**	0.072	**<0.001**	0.015	**0.042**
0.35	132.30	**<0.001**	0.196	0.073	0.247	0.068	0.261	0.084	0.051	**<0.001**	0.064	**<0.001**	0.014	**0.046**
0.4	131.41	**<0.001**	0.173	0.067	0.219	0.062	0.231	0.076	0.046	**<0.001**	0.058	**<0.001**	0.012	**0.049**
0.45	130.20	**<0.001**	0.154	0.061	0.196	0.057	0.207	0.070	0.042	**<0.001**	0.053	**<0.001**	0.011	**0.047**
0.5	129.18	**<0.001**	0.137	0.056	0.176	0.053	0.186	0.064	0.039	**<0.001**	0.049	**<0.001**	0.011	**0.045**
m = 5														
0.1	130.78	**<0.001**	0.484	0.153	0.592	0.150	0.625	0.204	0.109	**<0.001**	0.141	**<0.001**	0.032	**0.027**
0.15	133.99	**<0.001**	0.371	0.122	0.458	0.117	0.481	0.154	0.087	**<0.001**	0.110	**<0.001**	0.023	0.054
0.2	133.48	**<0.001**	0.303	0.103	0.376	0.098	0.395	0.125	0.073	**<0.001**	0.092	**<0.001**	0.019	0.053
0.25	133.36	**<0.001**	0.255	0.089	0.318	0.085	0.335	0.107	0.063	**<0.001**	0.080	**<0.001**	0.017	**0.045**
0.3	132.80	**<0.001**	0.220	0.079	0.275	0.075	0.290	0.094	0.055	**<0.001**	0.071	**<0.001**	0.015	**0.040**
0.35	131.65	**<0.001**	0.192	0.071	0.241	0.068	0.255	0.084	0.050	**<0.001**	0.063	**<0.001**	0.014	**0.043**
0.4	130.43	**<0.001**	0.169	0.065	0.214	0.062	0.226	0.075	0.045	**<0.001**	0.057	**<0.001**	0.012	**0.046**
0.45	128.72	**<0.001**	0.151	0.059	0.191	0.056	0.203	0.068	0.041	**<0.001**	0.052	**<0.001**	0.011	**0.042**
0.5	127.30	**<0.001**	0.135	0.055	0.172	0.052	0.183	0.062	0.037	**<0.001**	0.048	**<0.001**	0.010	**0.041**

F F-statistic, *SD* standard deviation, *MD* mean difference

Bold values indicate significant differences

Table 4.6: Linear measures of centre of pressure displacement by group

	Descriptive statistics by group						Post hoc					
	Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
Variable	Mean	SD	Mean	SD	Mean	SD	MD	p-value	MD	p-value	MD	p-value
Total displacement(cm)	110.479	71.097	152.342	96.961	162.718	102.772	41.863	**<0.001**	52.239	**<0.001**	10.376	0.266
Standard deviation, AP(cm)	0.730	0.347	0.833	0.434	0.866	0.446	0.103	**<0.001**	0.136	**<0.001**	0.033	0.519
Standard deviation, ML(cm)	0.511	0.279	0.639	0.401	0.683	0.440	0.128	**<0.001**	0.172	**<0.001**	0.044	0.251
Amplitude, AP(cm)	4.017	2.006	4.810	2.646	5.103	2.684	0.793	**<0.001**	1.086	**<0.001**	0.293	0.247
Amplitude, ML(cm)	2.930	1.669	3.663	2.357	3.889	2.575	0.733	**<0.001**	0.959	**<0.001**	0.226	0.337
Total Mean Velocity,(cm/s)	1.841	1.185	2.539	1.616	2.712	1.713	0.698	**<0.001**	0.871	**<0.001**	0.173	0.266
Mean velocity, AP(cm)	1.313	0.862	1.928	1.212	2.118	1.343	0.615	**<0.001**	0.805	**<0.001**	0.190	0.058
Mean velocity, ML(cm)	1.013	0.668	1.261	0.864	1.273	0.846	0.248	**<0.001**	0.26	**<0.001**	0.012	0.981
Area(cm^2)	8.270	7.481	12.710	13.015	14.250	14.326	4.440	**<0.001**	5.980	**<0.001**	1.540	0.155

SD standard deviation, *MD* mean difference, *AP* anterior-posterior, *ML* medial-lateral
Bold values indicate significant differences

4.4.3 Behaviour of sample entropy under the different testing conditions

For any given parameter combination, the mean SampEn value by group increased across the four testing conditions (vision-surface): OR < CR < OF < CF. Older adults showed higher mean SampEn values than young adults across all testing conditions, with Fallers consistently exhibiting higher mean values than Non-Fallers. The differences between older and young adults were found to be significant for all parameter combinations across testing conditions (Tables S8 to S11 in Appendix C). However, significant differences between Non-Fallers and Fallers were only found under the OF condition for two parameter combinations (see Table S10 in Appendix C). To illustrate these findings, Figure 4.7 shows the SampEn mean value and 95% confidence interval by group and testing condition for three selected parameter combinations, one of which produced significant differences between Fallers and Non-fallers ($m = 2$, $r = 0.1$, $N = 1200$).

4.5 Discussion

The use of ApEn and SampEn to characterise the regularity of CoP trajectories is still relevant. While previous studies have achieved promising results regarding the use of these entropy measures to discriminate between experimental groups and testing conditions, the adequate selection of input parameter values for the analysis of CoP time-series has not yet been formally investigated. This study aimed (1) to examine the effect of changing the values of parameters m, r and N on ApEn and SampEn values in CoP time-series, and (2) to determine the ability of ApEn and SampEn to discriminate between experimental groups. It was expected that ApEn and SampEn values would change significantly as functions of m, r and N, yet that SampEn would maintain consistent behaviour across different parameter value combinations (e.g. young adults showing consistently either higher or lower entropy values than older adults) [112]. Moreover, it was expected that significant differences in entropy values between young and older adults would be observed and that some parameter value combinations would potentially reveal significant differences between non-fallers and fallers.

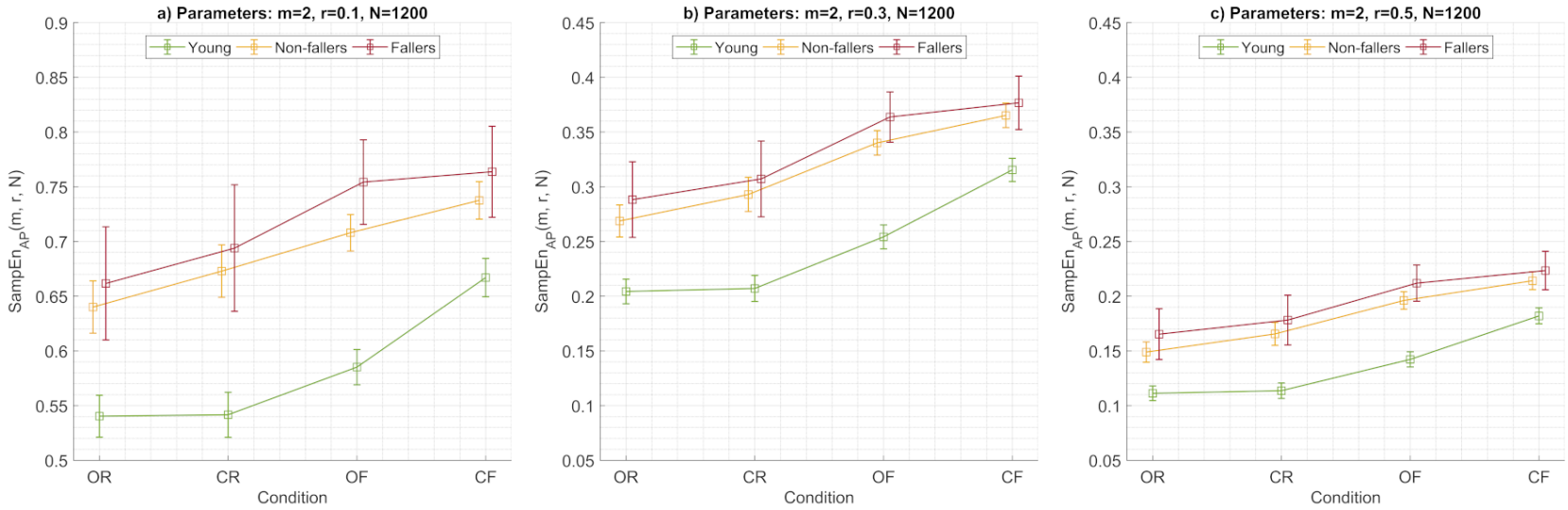

Figure 4.7: Sample entropy (SampEn) mean value (marker) and 95% confidence interval (error lines) by group and testing condition for selected parameter combinations. Conditions (vision-surface): *OR* open-rigid, *CR* closed-rigid, *OF* open-foam, *CF* closed-foam.

Firstly, the results confirm that the ApEn and SampEn algorithms are very sensitive to input parameter choice. Consequently, researchers and clinicians should be cautious when comparing studies using different parameters, even in similar populations and testing conditions: a direct comparison of entropy values (e.g. mean and range) should be completely avoided. However, the analyses in this study allow observation of the behaviour of ApEn and SampEn mean values over a wide range of input parameters, which might be useful for other studies. Namely, for a chosen m, both ApEn and SampEn tended to decrease as r increased, except in the case of ApEn for low values of r in combination with high values of m. The decreasing trend showed steeper slopes for lower values of m. Similarly, for a chosen r, ApEn and SampEn tended to decrease as m increased (Figure 4.4). In other words, CoP time-series exhibited more regularity (i.e. lower entropy values) for higher similarity tolerances and higher subseries lengths. The increase in regularity for higher values of r is an expected result, as it is a reasonable assumption that a higher number of subseries will meet the similarity criterion for a more relaxed tolerance. The increase in regularity for higher values of m suggests that patterns in CoP time-series are observed at larger time-scales rather than at smaller time-scales (e.g. in our study, $m = 5$ would correspond to a 0.25 to 0.3-second pattern and $m = 2$ to a 0.1 to 0.15-second pattern). This could presumably be linked to the well-known fact that for unperturbed standing posture the main components of the CoP signal are below 10 Hz [26]. As for the effects of data length, our results confirmed that ApEn is more dependent on this parameter than SampEn [111]. This claim is supported by the lower ApEn values observed for shorter time-series ($N = 600$) than for longer time-series ($N = 1200$). This situation is particularly evident for higher m values and lower r values. For instance, see Figure 4.4 and compare $ApEn_{AP}(m = 5, r = 0.1)$ for $N = 600$ (top left pane) to $N = 1200$ (top right pane); then compare $SampEn_{AP}(m = 5, r = 0.1)$ for $N = 600$ (bottom left panel) to $N = 1200$ (bottom right panel). Whereas a difference in the ApEn value between longer and shorter time-series is evident, the difference in the SampEn value is barely noticeable. These initial findings already tipped the scales in favour of SampEn when dealing with CoP time-series, in line with previous studies that had suggested their use for the analysis of cardiac inter-beat interval, gait and brain activity time-series [111, 112, 161]. Otherwise, they allow narrowing down the number of potentially useful input parameter combinations in case of using ApEn, discarding combinations of $m = \{4, 5\}$ and $r = \{0.1, 0.15, 0.2\}$.

Secondly, the results highlight issues with the relative consistency in CoP time-series for ApEn, as observed by the change in the direction of differences be-

tween groups (known as "flip" or "crossovers") for some combinations of m and r. For instance, in the AP direction older adults with falls in the last 12 months (Fallers) showed generally higher ApEn mean values than young adults, but the opposite trend was observed for $ApEn(m = 5, r = 0.1)$. This issue was still more evident when comparing older adults with and without falls in the last 12 months (i.e. Non-fallers and Fallers, respectively) as more combinations of m and r produce crossovers. Moreover, the issue with relative consistency was accentuated for shorter time-series ($N = 600$). Importantly, these issues were observed for higher values of m and lower values of r, which once again suggest that these values are not an optimal choice for CoP time-series analysis based on ApEn. In contrast, SampEn showed relative consistency, as no crossovers between groups were observed. This feature has been highlighted as one of the advantages of SampEn over ApEn for other types of biological data analysis as well [111, 112, 161]. This is an additional reason why researchers and clinicians should favour SampEn over ApEn for analysing CoP time-series.

Additionally, the results suggest that ApEn and SampEn are more sensitive than linear CoP displacement measures to differences between groups: ApEn and SampEn were able to discriminate between older adults with and without falls in the past 12 months (Tables 4.4 and 4.5), whereas linear measures were not (Table 4.6). In other words, while Non-fallers and Fallers exhibited commensurable CoP displacements in terms of magnitude (i.e. total length, amplitude and area), variability (i.e. standard deviation) and velocity (for instance, see Figure 4.1), they manifested differences in CoP time-series structure (more specifically, in regularity). Nevertheless, the results also revealed that the selection of input parameters in the computation of ApEn and SampEn is critical in the identification of significant differences between groups. Indeed, ApEn and SampEn were able to discriminate with ease between two highly heterogeneous groups, i.e. young and older adults, for a wide range of m, r and N values. However, only a subset of combinations revealed significant differences between more homogeneous groups; i.e., older adults with and without falls in the last 12 months. Those differences between groups were mainly observed for CoP time-series in the anterior-posterior direction with longer length ($N = 1200$, equivalent to a 60-second duration). Moreover, SampEn revealed significant differences for a higher number of combinations than ApEn. Therefore, it is suggested that researchers and clinicians aim to collect at least 60 seconds of posturography data and focus on the analysis of the anterior-posterior component of the CoP displacement using SampEn. However, it is appreciated that sustaining a quiet standing posture for more than 60 seconds can be challenging for some older

adults.

Furthermore, a more in-depth analysis of SampEn behaviour under four different testing conditions revealed that, while SampEn can discriminate with ease between two highly heterogeneous groups (i.e. young and older adults) for a wide range of testing conditions, some specific conditions might boost its sensitivity to differences between more homogeneous groups (i.e. older adults with and without falls in the last 12 months). Namely, older adults show significantly higher mean values than young adults across all testing conditions. However, significant differences between Non-Fallers and Fallers were only found for one condition; namely, the eyes open-foam surface condition (OF). Certainly, this was the case only for two parameter combinations. However, this fact might be explained by the imbalance in the dataset: there were 85 (53.5%) young adults, 56 (35.2%) non-fallers and only 18 (11.3%) fallers. These numbers have an important impact on inferential statistics: with a particularly low number of subjects in the Fallers group, the 95% confidence interval for the mean (Confidence Interval at 95% (CI)) of the group is expected to be wide, thus overlapping with the CI of the Non-fallers group. This situation is illustrated in 4.7, where SampEn mean values and CI by group and condition are shown for three selected parameter combinations. It can be observed that the 95%CIs for the Non-fallers and Fallers groups in the OF condition only partially overlap, suggesting that given a higher number of subjects in the Fallers group its CI would shrink, potentially producing non-overlapping CIs between those two groups. In contrast, the Non-Fallers and Fallers CI for other testing conditions are totally or almost overlapping, suggesting that they would remain so even if the size of the former group were higher. Similar results were observed across all values of m considered in the present study. Thus its choice seems to play a minor role in this specific aspect of analysis. However, the results suggest that the choice of r is critical, as higher values of r (e.g. $r = 0.5$) seem to distort the potentially distinctive profile line that each group shows for lower values (e.g. $r = 0.1$) when SampEn mean values are plotted across testing conditions. This observation allows narrowing further down the options of potentially useful values of r to somewhere in the middle of the range (e.g. $r = \{0.25, 0.3, 0.35\}$).

From the clinical perspective, the results provide researchers interesting insights. The first has to do with the direction of the difference in entropy values between the experimental groups in this study (i.e. young adults and older adults with and without recent falls). In the anterior-posterior direction, older adults (both fallers and non-fallers) exhibited significantly higher entropy values than young adults for most combinations of m, r and N. Moreover, Fallers exhibited generally higher

SampEn values than Non-Fallers (although that difference was significant only for some combinations of input parameters). Therefore, these findings conflict with the traditional interpretation of entropy values, which suggest that older adults should exhibit generally lower entropy values as a consequence of the loss of physiological complexity due to ageing and ill-health [162]. This conflict is solved by bearing in mind that entropy cannot be directly linked to complexity: a smaller entropy value does not mean less complexity, it only indicates more regularity based on one particular timescale [110, 111]. Therefore, if CoP entropy values observed in healthy young adults are to be taken as a reference, then the higher values found in older adults (especially in Fallers) may be indicative of posture control mechanisms that are too random to command balance properly. In other words, the irregularity observed in older adults might be associated with an unstructured system which becomes less sustainable [21]. As for CoP entropy values in the ML direction, the observed results resist a straightforward interpretation, as no significant differences between groups were found. However, the generally lower entropy values observed in Fallers compared to Young adults and Non-Fallers may suggest posture control mechanisms that are too stiff (too regular), which could be problematic when coping with external factors demanding an adaptable balance control. A second insight relates to the sensitivity of entropy measures to differences between groups compared to that of traditional measures. While the traditional measures were only able to discriminate between highly heterogeneous groups (young adults versus older adults), entropies could also discriminate between more homogeneous groups (non-fallers versus fallers). This suggests that Fallers suffer from balance impairments of a different nature to those produced by normal ageing. However, the elucidation of the specific nature of those impairments was beyond the scope of this study. A third insight relates to the conditions that seem to accentuate the differences in balance control mechanisms between the experimental groups. The findings suggest that neither the least nor the most challenging testing conditions (vision-surface: open-rigid and closed-foam, respectively) enable the discrimination of differences between Non-fallers and Fallers: both groups seem to cope similarly with those conditions. In contrast, a testing condition of intermediate complexity (i.e. open-foam) seems to better reveal those differences.

Finally, it must be acknowledged that there are more recent developments in the field of nonlinear analysis that could potentially improve the sensitivity when looking for differences between groups. In particular, the development of multiscale entropy and multivariate Multi-scale Entropy (MSE) have offered new perspectives for the analysis of biological time-series [163–166]. A few studies have already ap-

plied these approaches to the analysis of CoP time-series [99, 105, 107]. Briefly, these approaches rely on the computation of sample entropy values at different time-scales and produce a two-dimensional plot (time-scale versus sample entropy) depicting a profile line for each experimental group/condition. An overall entropy 'score' can be computed by adding the entropy values at specific time-scales [105]. While these new approaches represent an interesting tool to explore the level of regularity contained at different time-scales, they cannot avoid the issue of the adequate selection of input parameters. Since MSE and its variations are based on SampEn, the researchers and clinicians that opt for these newer approaches face essentially the same problem that those who opt for 'single-scale' entropy measures when it comes to input parameter selection. Hopefully, the present work will aid them in their choices or at least inspire them to adopt a systematic approach to the identification of the optimal parameters.

4.6 Conclusions

This chapter presented the secondary analysis of a public dataset of CoP time-series performed to investigate whether nonlinear descriptors, specially ApEn and SampEn, are more sensitive than linear measures to differences in balance control due to ageing and fall risk, as well as to identify the optimal way to apply them (e.g. signal pre-processing, selection of input parameters).

In summary, the results suggest that SampEn represents a better choice for the analysis of CoP time-series given its relative consistency and ability to discriminate between experimental groups. Nevertheless, the selection of input parameter values proved to be critical in the identification of significant differences between groups, in particular when those groups a presumably close to each other (in particular, older adults with and without falls in the last 12 months).

In particular, significant differences were mostly observed in CoP time-series in the AP direction of 60-s duration ($N = 1200$). Therefore, future studies using these entropy measures should favour longer CoP recordings (e.g. $\geq$ 60 seconds) over shorter CoP recordings (e.g. 30 seconds), as well as focus the analyses on AP time-series.

Additionally, significant differences between groups with a consistent trend were mostly observed for sample entropy. Hence, future studies should favour the use of the latter over approximate entropy. More specifically, when analysing the data regardless of testing condition, significant differences were observed for $SampEn(m = 2, r = \{0.4, 0.45, 0.5\})$ and $SampEn(m = \{4, 5\}, r = \{0.25, 0.3, 0.35, 0.4, 0.45, 0.5\})$.

Nevertheless, when analysing the data for specific testing conditions, higher values of r (≥ 4) distorted the seemingly distinctive pattern that each group showed when plotting SampEn mean values across testing conditions.

Finally, researchers and clinicians working on the analysis of CoP time-series are recommended: 1) to use SampEn with input parameters $m = \{4, 5\}$ and $r = \{0.25, 0.3, 0.35\}$, 2) to focus the analysis on the AP component, and 3) to further explore the 'eyes open-foam surface' testing condition as a potential booster of differences between groups.

This study led to the identification of optimal combinations of input parameters leading to discrimination between non-fallers and fallers using SampEn, thus answering the second research question underlying this thesis (see chapter 1). The study presented in the next chapter investigates potential associations between day-to-day variations in sleep quantity and quality, monitored using wearable devices, and balance in unperturbed standing. Hence, the study addresses the third research question.

Chapter 5

Day-to-Day Variations in Sleep Quality and Balance in Standing: the Role of Wearable Sensors

5.1 Chapter overview

Wearable devices are offering new opportunities for in-home continuous sleep monitoring in the broader population. They are potentially relevant for fall prevention, given that chronic sleep disturbances and poor sleep quality are associated with future falls in older people. Hence, if short-lived sleep disturbances and poor sleep quality have a similar effect on balance control, continuous sleep monitoring would be relevant for fall prevention programmes in frail populations and sleep disturbance-inducing scenarios (e.g. hospital wards). Therefore, the potential association between day-to-day variations in sleep quality and balance control deficits warrants investigation. This chapter presents a study that aimed to investigate the associations between day-to-day variations in sleep quality, measured via wearable devices, and balance in standing. Namely, this study investigated the potential use of wearable devices for monitoring day-to-day variations in sleep quantity and quality, as well as the sensitivity of the balance control system to these variations.

5.2 Introduction

Acute sleep deprivation is associated with alterations in posture control during quiet standing [167–177]. Balance deficits after intervals of 24 to 48 hours of sleep deprivation are reflected by wider [168, 171, 174–176], more fluctuating [167, 170, 172, 173] and faster [169] Centre of Pressure (CoP) displacements in the Anterior-Posterior (AP) axis. Moreover, vision plays a substantial role in static balance after 24 hours of sleep deprivation, as suggested by wider and more fluctuating CoP displacements observed when subjects are tested with eyes closed than when they are tested with eyes open [173]. After 26 hours of sleep deprivation, subjects also showed higher body sway under a single-task condition and lower body sway under a dual-task condition, suggesting that cognitive load also plays an essential role in balance control under sleep deprivation. These findings suggest that the effects of sleep deprivation on postural steadiness found under no cognitive load are compensated with a freezing strategy under cognitive load condition [175]. Moreover, older adults ($\geq$60 years old) suffer more sleep deprivation effects on balance than young adults (18–59 years old) [176]. This finding may be relevant in the context of fall prevention in senior citizens, especially in hospitalised older adults. Therefore, all these studies agreed that long periods of sleep deprivation ($\geq$24 h) are associated with deteriorations in static balance, especially in senior subjects.

More recently, the effects of chronic sleep restriction due to sleep debt and social jet lag have been studied [178, 179]. Chronic low sleep quality (i.e. higher sleep fragmentation and lower sleep efficiency) was found to affect balance control causing higher postural instability [178]. Moreover, social jetlag (i.e. the misalignment of the biological driven and socially dictated sleep times) was also found to deteriorate balance control [179], as suggested by posture control performance being consistently better on Mondays (after two of days of higher-quality sleep) than on Fridays (after a week of restricted sleep).

This chapter presents an experimental study performed to investigate the associations between day-to-day variations in sleep and balance. More specifically, this study investigates the potential use of wearable devices for monitoring day-to-day variations in sleep quantity and quality, as well as the sensitivity of the balance control system to these variations. The contents of this chapter have been published elsewhere [180].

5.3 Materials and methods

5.3.1 Study participants

Participants were recruited using e-mail advertising sent to postgraduate students from the School of Engineering of the University of Warwick. Exclusion criteria included having a medical history of sleep disorders, neurological or physical disabilities and having pharmacological treatment potentially affecting sleep patterns and postural control (e.g. anti-depressants, hypnotics and stimulants).

Baseline characteristics, such as age, height, weight, general health status and use of medications, were collected during a baseline assessment and briefing session. Participants were also asked to complete the Pittsburgh Sleep Quality Index (PSQI) instrument [30]. The PSQI questionnaire provided a global score computed from nineteen self-rated questions related to sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. The PSQI global score was used to compare baseline sleep quality over the past month between groups.

All subjects provided informed consent before participating in the study. The research protocol was approved by the Biomedical and Scientific Research Ethics Committee of the University of Warwick (REGO-2014-1039 AM01).

5.3.2 Equipment

Sleep monitoring was performed using the Zephyr BioHarness 3.0 (Medtronic, Inc., Annapolis, MD, USA), a wearable device that measures tri-axial trunk acceleration and one-lead Electrocardiogram (ECG) signals at a sampling frequency of 100 Hz and 1 kHz, respectively, at a resolution of 12 bits per sample (Figure 5.1). The device is attached to chest over the xiphoid process (i.e. the bone structure located at the centre to the chest, below the lower part of the sternum) using a pair of pre-gelled, disposable electrodes. This device uses proprietary algorithms to calculate the user's activity level and posture based on acceleration signals. Activity level is reported in gravitational force units (i.e. g-force or simply g, where $1g = 9.806m/s^2$) within a range of 0 to 16 g and is computed as

$$Activity = \sqrt{x^2 + y^2 + z^2} \tag{5.1}$$

where x, y and z are the average acceleration for the vertical, medial-lateral and anterior-posterior axes, respectively, over 1-second, non-overlapping windows. Posture is the wearer's angle of deviation from the vertical axis, where 0°=subject

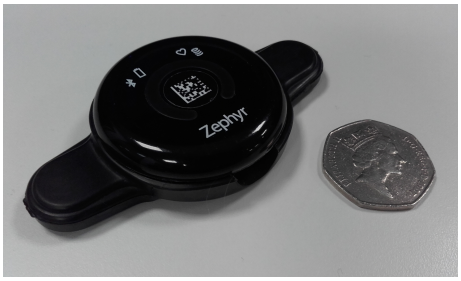

Figure 5.1: Wearable device used for sleep monitoring

vertical, 90°=subject prone (face down) and -90°=subject supine (face up) Activity and Posture time-series are reported with a frequency of 1 sample per second. Moreover, this device performs R peak detection on the ECG waveform and reports R-R intervals in milliseconds. Raw three-axial accelerations, ECG signals, R-R interval time-series, and a summary file containing the activity and posture time-series are stored in the internal memory of the device during use and can be downloaded for further processing. The validity and reliability of the Zephyr BioHarness are strong to very strong for heart rate, acceleration and posture monitoring at low to moderate physical activity levels [181, 182]. Figure 5.2 shows representative activity and posture signals during sleep.

Balance assessment was performed using the Tekscan F-Scan system (Tekscan, Inc., South Boston, MA, USA), a plantar pressure measurement and analysis system. This system is based on a pair of ultra-thin (0.15mm) instrumented insoles with a spatial resolution of 3.9 pressure-sensing elements per cm^2. Bi-plantar pressure data were collected at a rate of 200 frames per second. Based on pressure data, the F-Scan Research 7 software computes the foot CoP location for each frame. CoP displacement is stored as a time-series of numerical data in the AP and Medial-Lateral (ML) axes in relation to the orientation of the subject. Figure 5.3 shows a representative bi-plantar pressure distribution map during quiet standing and the resulting centre of pressure displacement trajectory. According to the manufacturer's recommended procedures, the F-Scan system was calibrated for each participant following the point calibration routine, the suggested method for standing balance trials. This calibration procedure requires each sensor to be individually calibrated by having the subject standing on a single foot at a time for a few seconds (≈5 seconds). Hsiao *et al.* emphasised the importance of calibrating the system in actual experimental conditions before use [183]. Providing that the proper calibration procedure is followed, the accuracy of the F-Scan system has been found to be satisfactory (i.e., with a measurement error of less than 6%) when the

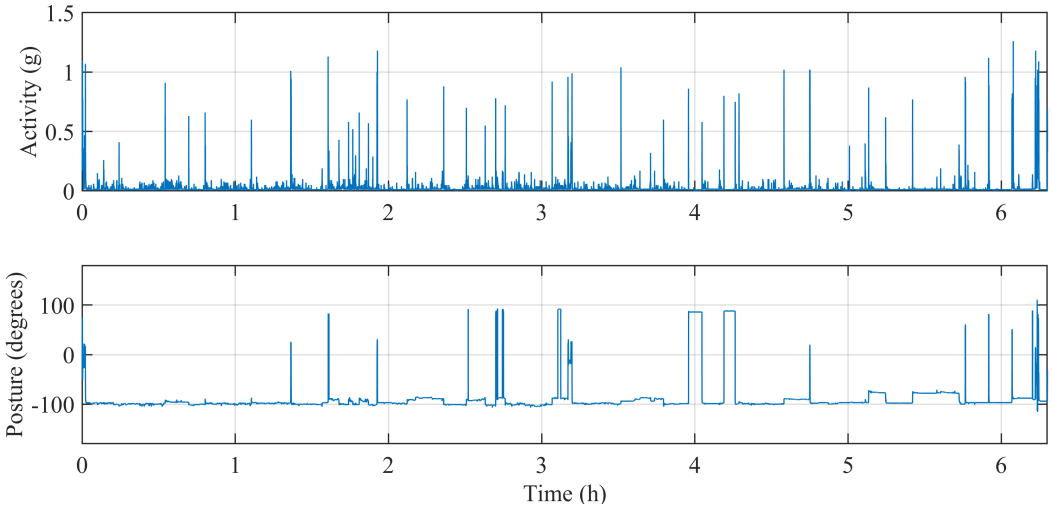

Figure 5.2: Activity (top) and posture (bottom) signals during sleep for a participant that reported poor sleep quality. Activity level is expressed in gravitational force units with a range from 0 to 16 g (1 g = 9.806 m/s^2). Posture is the wearer's angle of deviation from the vertical axis, where 0°=subject vertical, 90°=subject prone (face down) and -90°=subject supine (face up). Data collected by the author as part of this study.

sensors are subjected to static loads (e.g. during quiet standing) and the pressure applied during the protocol is comparable with that used during calibration [183]. These considerations are worth mentioning, as some studies have questioned the validity and reliability of the Tekscan F-Scan system, when utilised with dynamic loads (i.e. walking [184]) or when the sensors were calibrated using two pressure values and tested over a broader range [185].

5.3.3 Study protocol

A schematic of the study protocol is depicted in Figure 5.4. After baseline assessment, participants underwent sleep and balance assessment for two consecutive days. For sleep assessment, they were asked to wear the BioHarness during sleep; i.e., to apply it at the time of usual bedtime and to take it off after the final awakening. Additionally, subjects were required to complete the Consensus Sleep Diary (CSD) every morning immediately after getting out of bed during their participation in the study [31]. Participants were invited to stick to their regular sleep schedule and habits (i.e. no intervention was applied).

Balance was assessed in two morning sessions starting at the same time of the day (9:00 or 10:00 a.m.) for any given participant. Previous studies have suggested

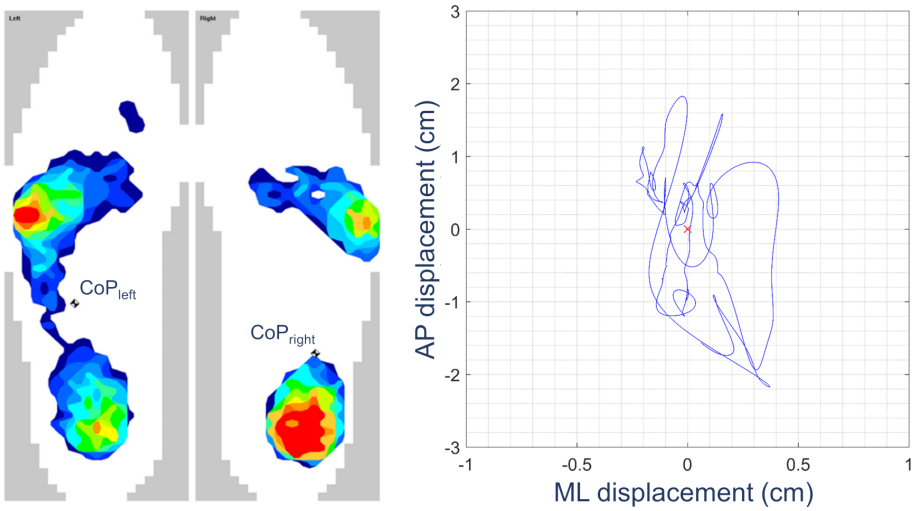

Figure 5.3: Plantar pressure map and centre of pressure (CoP) trajectory. Left: Representative bi-plantar pressure map during quiet standing. The black and white circle represents the foot CoP computed from pressure distribution data. Right: Representative centre of pressure trajectory (left foot) for a 20-second window. Data collected by the author as part of this study.

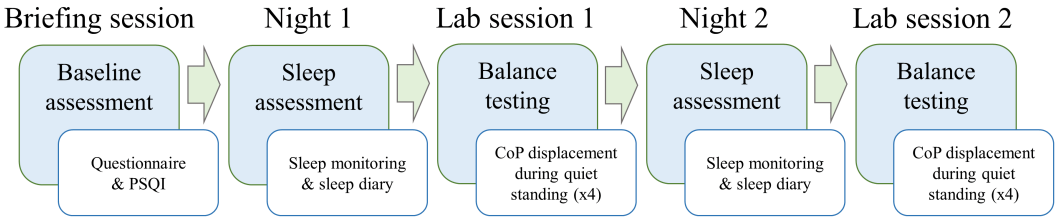

Figure 5.4: Schematic diagram of the study protocol. Sleep monitoring was performed using a wearable device that records acceleration and electrocardiogram signals. Balance assessment was performed using a plantar pressure measurement and analysis system based on a pair of instrumented insoles.

that CoP measures vary throughout the day, allegedly following a circadian pattern [168–170]. By starting both sessions at the same time of the day, the influence of time of day on CoP measures was discarded as a potential confounder. At each session, participants were asked to complete four quiet standing trials with eyes open. Namely, they were instructed to stand quietly on the foot pressure sensors with arms hanging naturally at their sides and eyes staring at a fixed point on the wall in front of them. The sensors were attached to the floor side-by-side in a comfortable position for each participant (about shoulder width). The duration of each trial was 30 seconds and a brief resting interval (≈15 seconds) was allowed between trials. Participants wore socks but no shoes during the session.

5.3.4 Data processing

Data collected via the sleep diary, the BioHarness and the Tekscan system were processed as follows in order to compute a set of sleep and balance measures (see Table 5.1 for a summary of those measures with their definitions).

5.3.4.1 Sleep diary measures

Five sleep measures were extracted from the sleep diary: 1) Sleep Onset Latency (SOL); 2) Wake After Sleep Onset (WASO), a measure of sleep fragmentation; 3) Total Sleep Time (TST) or sleep duration; 4) Sleep Efficiency (SE), and; 5) Subjective Sleep Quality (SSQ). The definition of these measures can be found in Table 5.1.

5.3.4.2 Sleep activity level measures

Activity level signals were processed to compute six measures of activity during sleep (Figure 5.5). Firstly, raw signals were trimmed based on posture data to discard activity data outside the sleep period (i.e. before getting into and after getting out of bed). Then, the signals were segmented into continuous, non-overlapping 1-minute epochs and activity counts were computed for each epoch using the zero-crossing mode, described in section 2.5; i.e., the activity level was compared with the reference activity level, and each threshold crossing generated an activity count [124]. The threshold was set to 0.1 g for high sensitivity. This generated a time-series $\langle ACT(n) \rangle$ with the form

$$\langle ACT(n) \rangle = ACT(1), ACT(2), \ldots, ACT(N)$$

where $ACT(i)$ is the number of activity counts for the 1-minute i^{th} 1-minute epoch and N is the total number of 1-minute epochs.

Subsequently, an *inactive interval* was defined as a sequence of two or more consecutive epochs whose number of activity counts is equal to zero. Based on this definition, the $\langle ACT(n) \rangle$ was examined to determine the number and duration of inactive intervals, which produced a time-series $\langle I(m) \rangle$ of the form

$$\langle I(m) \rangle = I(1), I(2), \ldots, I(M)$$

where $I(j)$ is the duration (minutes) of the j^{th} inactive interval and M is the total number of inactive intervals.

Finally, six activity measures were computed (Table 5.1):

1. Mean activity counts per epoch

$$ACT_{mean} = \frac{1}{N} \sum_{i=1}^{N} ACT(i) \tag{5.2}$$

2. Standard deviation of activity counts per epoch

$$ACT_{sd} = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N} \left[ACT(i) - \frac{1}{N} \sum_{i=1}^{N} ACT(i) \right]^2} \tag{5.3}$$

3. Activity index, defined as the percentage of epochs that the participant was active (i.e. activity counts>0)

$$AI = \frac{\text{number of } ACT(i) > 0}{N} \times 100 \qquad \forall i \tag{5.4}$$

4. Fragmentation index, defined as the percentage of inactive intervals with duration of less than or equal to 5 minutes

$$FI = \frac{\text{number of } I(j) \leq 5}{M} \times 100 \qquad \forall j \tag{5.5}$$

5. Duration of the longest inactive interval

$$I_{max} = \max I(i) \tag{5.6}$$

6. Mean duration of the inactive intervals

$$I_{mean} = \frac{1}{M} \sum_{j=1}^{M} I(j) \tag{5.7}$$

These measures were computed using in-house written scripts in MATLAB R2017b (The Mathworks, Inc., Natick, MA, USA). The source code can be found in Appendix A.

5.3.4.3 Heart rate variability measures

Heart Rate Variability (HRV) measures were computed from R-R time-series in order to characterise autonomic cardiac modulation during sleep (Figure 5.5). As mentioned in section 2.5, a higher parasympathetic tone has been observed during Non-Rapid Eye Movement (NREM) sleep, especially during deep sleep; in contrast, a higher sympathetic tone has been observed during wake intervals, Rapid Eye Movement (REM) sleep and sleep arousals [35]. Therefore, the HRV analysis provided with an indication of the presence of wake intervals and arousals, as well as of shorter deep sleep periods.

Firstly, the R-R series were segmented based on posture data to discard heartbeats outside the sleep period. Subsequently, the software HRVanalysis was used to correct R-R time-series and compute four HRV measures from them: two frequency-domain measures (Low-Frequency (LF) and High-Frequency (HF) power) and two nonlinear measures (Approximate Entropy (ApEn) and Sample Entropy (SampEn)) [186]. The automatic R-R interval correction algorithms involve two steps. First, spurious R-R intervals are detected based on the relative variation in successive intervals: R-R intervals with a variation of +32.5% or -24.5% are considered to be spurious and thus discarded [187]. Second, discarded R-R intervals are recalculated as follows: if the number of successive false R-R intervals is 3 or less, these are recalculated by cubic spline interpolation; otherwise, they are replaced by copying the same number of previous valid R-R intervals [186]. In addition, three frequency-domain measures were computed using in-house written scripts in MATLAB R2017b: LF normalised, HF normalised and LF/HF ratio. The meaning of these HRV measures has been widely described in literature [126, 127]. In the context of sleep assessment, those features are associated with specific sleep stages and other relevant phenomena (e.g. arousals) [126]. In the frequency-domain, HF power describes the parasympathetic activity, whereas LF power describes both parasympathetic and sympathetic activity. Thus, the relationship between both branches

usually is explored with the normalised frequency values and the LF/HF ratio. A higher LF/HF ratio reflects a higher HRV. Finally, entropy measures represent an index of regularity in the cardiac signal. An increase in regularity (i.e., an increase in the entropy measure) is associated with parasympathetic modulation, and its decrease is interpreted as the result of an increased sympathetic tone.

5.3.4.4 Balance measures

A block diagram depicting the steps followed for the CoP data processing is shown in Figure 5.6. CoP time-series were segmented to discard the initial and last 5 seconds of each trial in order to account for the adaptation phase of the participant to the quiet standing task and the effects of fatigue or lack of attention associated with a sustained task, respectively [188]. Subsequently, the CoP time-series were passed through a fourth-order, zero-phase Butterworth low-pass digital filter with a cut-off frequency of 5 Hz in order to remove acquisition noise. This cut-off frequency was selected since most of the components of CoP signals are below this frequency [189]. Afterwards, they were detrended (i.e., subtraction of the mean value from the time-series). Hence, the analysis of the CoP displacement was carried out relative to its mean position and not to the origin of the sensors' coordinate system. Finally, three CoP displacement measures were computed as described in detail in section 2.4: area, amplitude and standard deviation. These measures were computed for left and right feet independently. Additionally, the measures for left and right feet were averaged. Amplitude and standard deviation were computed in the AP axis only, as previous studies have shown that it is mainly on this axis that balance alterations are observed [171, 173, 175, 176]. The definition of these measures is presented in Table 5.1.

Scripts for CoP data processing were also written in MATLAB R2017b. The source code can be found in Appendix A.

Table 5.1: Summary of sleep and centre of pressure displacement measures

Measure	Units	Description
Sleep measures		
Sleep diary measures		
Sleep onset latency (SOL)	minutes	Duration of the transition interval from wakefulness to sleep.
Wake after sleep onset (WASO)	minutes	Total duration of intervals of wakefulness between sleep onset and final awakening. It is a measure of sleep fragmentation.
Total sleep time (TST)	h	Total duration of actual sleep
Sleep efficiency (SE)	%	Ratio of total sleep time to time-in-bed expressed as a percentage
Subjective sleep quality (SSQ)	-	Subjective appraisal of quality of sleep (1=Very poor, 2=Poor, 3=Fair, 4=Good, 5=Very good)
Activity level measures		
ACT_{mean}	counts	Mean activity counts per epoch over the entire sleep opportunity
ACT_{sd}	counts	Standard deviation of activity counts per epoch over the entire sleep opportunity
Activity Index (AI)	%	Percentage of 1-minute epochs with activity counts >0
Fragmentation Index (FI)	%	Percentage of inactive intervals with duration $\leq$ 5 minutes
I_{max}	minutes	Duration of the longest inactive interval
I_{mean}	minutes	Average duration of all inactive intervals

Table 5.1 continued from previous page

Measure	Units	Description
HRV measures		
LF	ms^2	Power in the low-frequency range (0.04-0.15 Hz)
HF	ms^2	Power in the high-frequency range (0.15-0.4 Hz)
LF normalised	-	LF power in normalised units, computed as LF / LF+HF x 100
HF normalised	-	HF power in normalised units, computed as HF / LF+HF x 100
LF/HF ratio	-	Ratio LF to HF
Approximate entropy (ApEn)	-	A measure of the regularity or self-similarity of fluctuations in the R-R time-series
Sample entropy (SampEn)	-	A modification of ApEn that reduces the chances to overestimate the entropy in a time-series
CoP displacement measures		
Area	cm^2	Area of the ellipse that contains 95% of the CoP points
Amplitude	cm	Distance between the minimum and maximum positions. Also known as range.
Standard deviation	cm	Dispersion of the CoP position around the mean

HRV heart rate variability, *CoP* centre of pressure

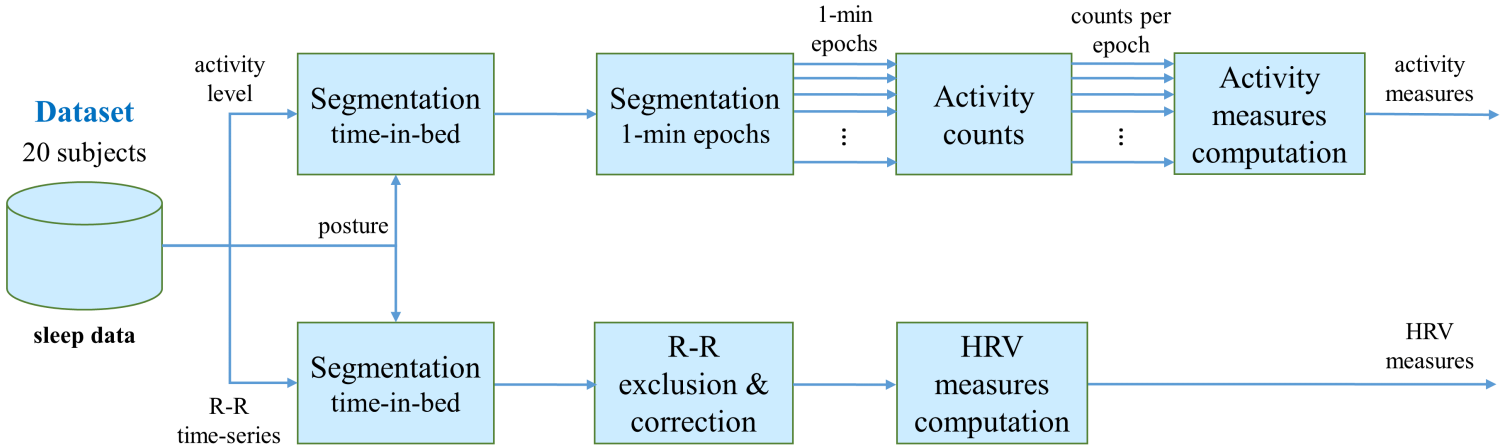

Figure 5.5: Block diagram of sleep data processing. Activity level time-series were trimmed based on posture data to discard intervals outside the sleep period. Then, the time-series were segmented in continuous, non-overlapping 1-minute epochs and activity counts were computed for each epoch. Finally, six measures of activity were computed for each epoch. R-R time-series were also trimmed based on posture data. Then, seven heart rate variability measures were computed in order to characterise autonomic cardiac modulation during sleep.

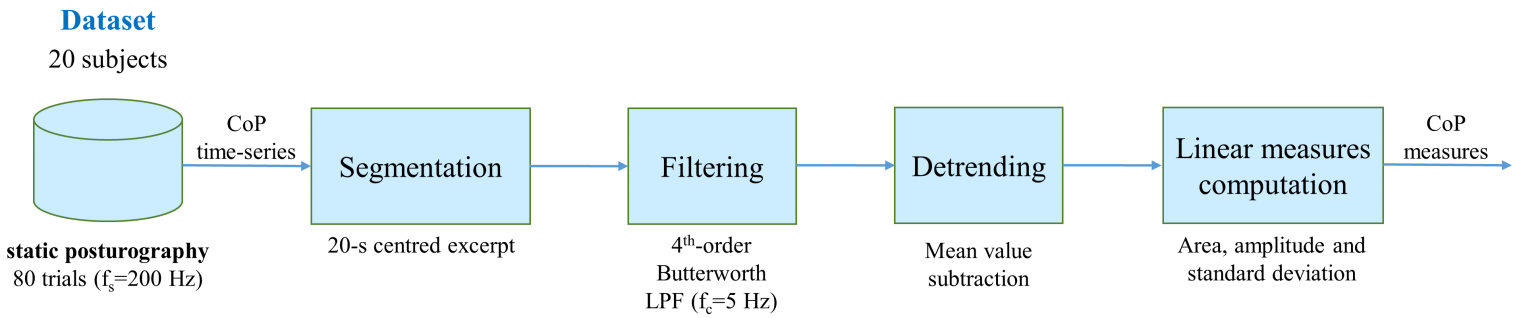

Figure 5.6: Block diagram of centre of pressure (CoP) data processing. CoP time-series were segmented to discard the initial and last 5 seconds of each trial. Then, the CoP time-series were filtered to remove acquisition noise and detrended. Finally, three CoP displacement measures were computed.

5.3.5 Statistical analysis

Participants were grouped based on the sleep quality scores they reported in the sleep diary (i.e. SSQ). Participants who reported no variation in sleep quality over two consecutive nights were assigned to the *Control group*. Participants who reported a variation in sleep quality over two consecutive nights (e.g. good sleep quality in one night and poor sleep quality in the other) were assigned to the *Case group*. The validity of self-reported sleep quality was tested by running pairwise comparisons for all other sleep measures within each group. By definition, no differences over consecutive nights were expected for the *Control group*, while significant differences were expected for the *Case group*. Two-sided Wilcoxon paired tests with a significance level set at 0.05 were used for these comparisons, given that most sleep measures exhibited a non-normal distribution (Table 5.2).

Subsequently, a repeated measures Analysis of Variance (ANOVA)-type rank test for factorial designs was performed in order to test the main effects and the interaction effects of *Group* and *Session* on balance measures [190]. This test was developed for experimental designs where subjects are stratified in several groups, as well as observed at different time points (i.e., mixed designs). Importantly, these tests are robust to outliers and small sample sizes. The computational implementation of this test provided by the authors via the R package nparLD version 2.1 was used [191]. The main effects and interaction effects of *Group* and *Session* were tested for all balance measures. A p-value < 0.05 was accepted as indicative of statistical significance. This analysis was performed in R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Finally, differences in balance measures between sessions were investigated for each group (i.e. *post hoc* comparisons): for the *Control group*, pairwise comparisons were always made between Session 2 and Session 1, given that by definition for this group sleep quality was equally rated in both sleep opportunities; for the *Case group*, pairwise comparisons were made between the session with the poorest sleep quality and the session with the best sleep quality, regardless of the chronological order in which they were presented. Two-tailed Wilcoxon paired tests were performed given the non-normal distribution of most balance measures (Shapiro-Wilk test with a p-value < 0.05). A p-value < 0.05 was accepted as indicative of statistical significance. These tests were conducted in MATLAB R2017b.

Table 5.2: Normality test on sleep measures. A Shapiro-Wilk test of normality was performed on the sleep measures. P-values < 0.05 (bold) suggest that there is evidence that the data tested were not normally distributed.

Measure	W-statistic	p-value
Sleep diary measures		
SOL	0.66	**0**
WASO	0.59	**0**
TST	0.97	0.351
SE	0.92	**0.011**
Activity level measures		
ACT_{mean}	0.87	**0.001**
ACT_{sd}	0.93	**0.020**
AI	0.85	**0**
FI	0.97	0.491
I_{max}	0.94	0.056
I_{mean}	0.98	0.741
HRV measures		
LF	0.87	**0.001**
HF	0.67	**0**
LF normalised	0.95	0.103
HF normalised	0.95	0.103
LF/HF ratio	0.89	**0.003**
ApEn	0.99	0.938
SampEn	0.98	0.547

SOL sleep onset latency, *WASO* wake after sleep onset, *TST* total sleep time, *SE* sleep efficiency, *HRV* heart rate variability, *LF* low-frequency power, *HF* high-frequency power, *ApEn* approximate entropy, *SampEn* sample entropy

5.4 Results

5.4.1 Participants baseline characteristics and stratification

Twenty volunteers (12 females and 8 males) participated in this study. The sample had an overall mean (standard deviation) age of 28.8 (5.7) years, height of 170.8 (8.3) cm, mass of 68.7 (13.2) kg, body mass index of 23.4 (3.4) kg/m^2, heart rate at rest of 63.1 (8.7) beats/minute, PSQI score of 5.1 (2.4) and average sleep duration of 7 (1) hours during the past month. No significant differences were found between groups for these characteristics (Table 5.3).

Six participants reported no variation in sleep quality over two consecutive nights (*Control group*), whereas 14 participants reported a variation in sleep quality over two consecutive nights (*Case group*). No significant differences were found in sleep measures over the two consecutive nights for the *Control group*. Conversely, the *Case group* exhibited significant differences for some sleep measures (Table 5.4). Namely, for the poorest sleep quality night (i.e., the lowest-rated) the *Case group* exhibited:

- Longer WASO (p=0.043) and shorter TST (p=0.038), as self-reported in the sleep diary.
- Higher mean and standard deviation of activity counts per epoch (p=0.033 and p=0.048, respectively), higher activity index (p=0.033) and shorter mean duration of the more extended inactive interval (p=0.041) as computed from the trunk acceleration signals.
- Lower heart rate variability, as reflected by lower power in the HF band (p=0.033) and lower ApEn and SampEn (p=0.021 and p=0.006, respectively).

5.4.2 Group and Session main effects and interaction effects on balance measures

The main effects of *Group* and *Session* were not significant for any CoP displacement measure (Table 5.5). However, two CoP displacement measures showed significant *Group*Session* interaction effects:

- Area of displacement for the right foot (p=0.025)
- Standard deviation (AP axis) for the right foot (p=0.017)

Table 5.3: Baseline characteristics of study participants. Mean and standard deviation for all subjects, subjects without day-to-day variation in sleep quality (*Control group*) and subjects with variation in day-to-day sleep quality (*Case group*). P-values from two-tailed paired t-tests are also shown.

	All (n = 20)		Control group (n = 6)		Case group (n = 14)		
Variable	Mean	SD	Mean	SD	Mean	SD	p-value
Age (years)	28.8	5.7	29.5	5.7	28.4	5.9	0.711
Mass (kg)	68.7	13.2	64.3	11.3	70.6	13.9	0.339
Height (cm)	170.8	8.3	167.6	6.8	172.1	8.8	0.279
BMI (kg/m^2)	23.4	3.4	22.8	3.7	23.7	3.4	0.608
HR (bpm)	63.1	8.7	63.4	8.2	63.0	9.2	0.925
PSQI	5.1	2.4	5.0	1.7	5.1	2.7	0.908
TST (hours)	7.0	1.0	7.2	1.0	7.0	1.1	0.727

SD standard deviation, *BMI* body mass index, *HR* heart rate at rest, *PSQI* Pittsburgh Sleep Quality Index, *TST* total sleep time for the past month

5.4.3 Pairwise comparisons for balance measures

As reported in Table 5.6, eight CoP displacement measures exhibited significant differences after sleep deterioration (*Case group*). Namely, after the lowest-rated sleep participants showed a less stable balance as reflected by:

- an increase in the area of displacement for left and right feet, as well as for the averaged measure (p=0.049, p=0.011 and p=0.035, respectively)
- an increase in the amplitude of displacement (AP axis) for left and right feet, as well as for the averaged measure (p=0.025, p=0.013 and p=0.020, respectively)
- an increase in standard deviation (AP axis) for the right foot and the average for both feet (p=0.035 and p=0.042, respectively)

Conversely, no significant CoP displacement measure variations were observed in the *Control group* (i.e., subjects presenting no sleep quality variations). Figure 5.7 illustrates the observed results for the feet-averaged CoP displacement measures.

5.5 Discussion

This study investigated the potential use of wearable devices for monitoring day-to-day variations in sleep quantity and quality, as well as the sensitivity of the

balance control system to these variations. The hypothesis was that balance in unperturbed standing, measured by foot CoP displacement, may be affected by changes in sleep quantity and quality over two consecutive nights. Firstly, the study explored whether day-to-day self-reported sleep quantity and quality was confirmed by instrumented sleep assessment using wearable devices. Therefore, participants were divided into two groups based on whether or not they reported a shift in sleep quality over two consecutive nights. Importantly, reported changes in sleep quality were not artificially induced; they were instead the consequence of spontaneous sleep disturbances experienced during the lowest-rated sleep opportunity (e.g. the need to use the toilet, an uncomfortable room temperature and involuntarily waking up in the middle of the night or early in the morning for no apparent reason, among the most referred disturbances). Subjects reporting a shift in sleep quality reported significantly higher sleep fragmentation (WASO) and significantly lower sleep duration (TST) for the lowest-rated sleep opportunity. They also showed higher levels of activity and shorter inactive intervals as measured via body acceleration signals, suggesting a less quiet and more fragmented sleep. These results suggest that self-reported sleep quality was indeed associated with a shorter, more discontinuous and less quiet sleep, in line with the study by Furtado *et al.* [178], in which higher WASO and activity levels were observed in subjects with low-quality sleep over one week. Moreover, in the present study, subjects reporting a variation in sleep quality also exhibited higher sympathetic activity (i.e., lower heart rate variability) during the sleep opportunity, which according to existing literature suggests the presence of more wake intervals and/or arousals, and fewer and/or shorter deep sleep intervals [35]. All these differences confirmed that the subjective sleep quality appraisal that participants made via the sleep diary reflected actual variations in objective sleep measures. Therefore, wearable devices can be used to detect day-to-day variations in sleep quantity and quality.

Table 5.4: Day-to-day differences in sleep measures. Median difference and interquartile range of the median difference subjects without day-to-day variation in sleep quality (*Control group*) and subjects with variation in day-to-day sleep quality (*Case group*). P-values from two-tailed paired Wilcoxon tests are also shown.

	Control group (n = 6)			Case group (n = 14)			
Measure	MD	IQR	p	MD	IQR	p	Trend
Sleep diary measures							
SOL (min)	-7.5	20	0.656	2.5	17	0.386	↑
WASO (min)	-0.5	5	0.375	4	10	**0.043**	↑↑
TST (h)	-0.5	1.5	0.250	-0.675	1.83	**0.038**	↓↓
SE (%)	2.5	5	0.438	-1.5	10	0.236	↓
Activity level measures							
ACT_{mean} (counts)	-0.045	0.097	0.438	0.024	0.109	**0.033**	↑↑
ACT_{sd} (counts)	-0.045	0.227	0.219	0.075	0.266	**0.048**	↑↑
AI (%)	-1.514	4.978	0.313	0.793	4.149	**0.033**	↑↑
FI (%)	-3.199	12.433	0.156	3.571	13.166	0.735	↑
I_{max} (min)	-13	30	0.219	-9	22	**0.041**	↓↓
I_{mean} (min)	1.575	6.764	0.844	-1.416	4.49	0.191	↓
HRV measures							
LF (ms^2)	52.556	767.843	0.438	-238.447	615.061	0.146	↓
HF (ms^2)	-44.143	231.888	1	-115.617	241.026	**0.033**	↓↓
LF normalised	0.689	6.171	1	2.323	8.165	0.127	↑
HF normalised	-0.689	6.171	1	-2.323	8.165	0.127	↓
LF/HF ratio	0.188	1.095	0.844	0.323	1.745	0.191	↑
ApEn	-0.001	0.050	1	-0.037	0.059	**0.021**	↓↓
SampEn	0.034	0.149	0.844	-0.042	0.109	**0.006**	↓↓

MD median difference, *IQR* interquartile range, p p-values from two-tailed paired Wilcoxon tests, *SOL* sleep onset latency, *WASO* wake after sleep onset, *TST* total sleep time, *SE* sleep efficiency, *HRV* heart rate variability, *LF* low-frequency power, *HF* high-frequency power, *ApEn* approximate entropy, *SampEn* sample entropy
Bold values indicate significant differences
↓↓ (↑↑): significantly lower (higher) for poorer sleep quality night
↓ (↑): lower (higher) for poorer sleep quality night

Table 5.5: Main effects and interaction effects of *Group* and *Session* on balance measures.

Factor / Interaction	Group		Session		Group*Session	
Measure	Fn		Fn	p	Fn	p
Area, left foot	0.096	0.757	1.427	0.232	0.603	0.437
Area, right foot	0.086	0.770	0.029	0.866	5.027	**0.025**
Area, average	0.062	0.804	0.310	0.578	0.734	0.392
Amplitude, AP, left foot	0.118	0.731	0.982	0.322	0.271	0.603
Amplitude, AP, right foot	0.242	0.623	1.867	0.172	3.243	0.072
Amplitude, AP, average	0.074	0.786	3.652	0.056	0.989	0.320
Standard deviation, AP, left foot	0.032	0.859	0.436	0.509	0.901	0.342
Standard deviation, AP, right foot	0.211	0.646	0.002	0.962	5.656	**0.017**
Standard deviation, AP, average	0.049	0.824	0.637	0.425	2.550	0.110

AP anterior-posterior, *Fn* ANOVA-type statistic, p p-values from ANOVA-type non-parametric two-tailed paired tests.
Bold values indicate significant interactions

Table 5.6: Day-to-day differences in centre of pressure displacement measures. Median difference and its interquartile range for subjects without day-to-day variation in sleep quality (*Control group*) and subjects with variation in day-to-day sleep quality (*Case group*).

	Control group (n = 6)			Case group (n = 14)			
Measure	MD	IQR	p	MD	IQR	p	Trend
Area, left foot (cm^2)	0.014	0.248	0.688	0.048	0.281	**0.049**	↑↑
Area, right foot (cm^2)	-0.049	0.207	0.313	0.031	0.176	**0.011**	↑↑
Area, average (cm^2)	0.003	0.550	0.844	0.042	0.239	**0.035**	↑↑
Amplitude, AP, left foot (cm)	0.248	0.437	0.563	0.319	1.693	**0.025**	↑↑
Amplitude, AP, right foot (cm)	-0.066	0.969	0.844	0.228	0.609	**0.013**	↑↑
Amplitude, AP, average (cm)	0.091	0.343	0.688	0.252	1.121	**0.020**	↑↑
Standard deviation, AP, left foot (cm)	0.006	0.099	0.844	0.056	0.364	0.058	↑
Standard deviation, AP, right foot (cm)	-0.032	0.089	0.438	0.046	0.217	**0.035**	↑↑
Standard deviation, AP, average (cm)	0.005	0.120	1	0.048	0.283	**0.042**	↑↑

AP anterior-posterior, *MD* median difference, *IQR* interquartile range, p p-values from two-tailed paired Wilcoxon tests
Bold values indicate significant differences
↓↓ (↑↑): significantly lower (higher) for poorer sleep quality night
↓ (↑): lower (higher) for poorer sleep quality night

The main effects and the interaction effects of *Group* and *Session* on balance measures were tested. No significant *Group* or *Session* main effects were found for any CoP measure, confirming the overall homogeneity in balance performance between groups and sessions. Conversely, two CoP displacement measures showed significant *Group*Session* interactions, confirming the hypothesis that day-to-day variations in balance are associated with variations in sleep quantity and quality over consecutive nights.

The *Group*Session* interaction effects above were found to be attributable to subjects that exhibited a variation in sleep quantity and quality over consecutive nights. The group of subjects reporting and exhibiting worsening in sleep measures over two consecutive days also exhibited larger CoP displacements (i.e., amplitude and area) and fluctuations (i.e., standard deviation), particularly in the anterior-posterior axis. These results are in line with previous studies, which have also found larger, more fluctuating and faster CoP displacements in the anterior-posterior axis as a result of 24 to 48 hours of sleep deprivation [167–176]. This suggests that the alterations in postural control observed after a day-to-day deterioration in sleep quality have similar manifestations (direction) to those produced by more extended periods of sleep deprivation. These alterations could potentially increase (in magnitude) in older adult populations, as suggested by a previous study where the effects of sleep loss on balance measures were found to be modulated by age, with older adults showing an increase in CoP speed more than twice higher than younger adults after sleep deprivation [176]. However, this observation requires further investigation.

Altogether, these results confirm that day-to-day variations in sleep quality are associated with variations in static balance among healthy young adults. The fact that no differences were found in the group of participants that reported and exhibited no differences in sleep quality over two nights supports this conclusion.

The neurophysiological mechanisms behind the observed alterations in postural control need to be elucidated. It is known that both vigilant attention and the visual system are affected by sleep deprivation [192–195]. Both have also been found to play an essential role in postural control [40, 196–199]. Future studies could further investigate the effects of day-to-day variations in sleep quantity and quality, and standing balance by observing its modulation by available attentional resources (e.g. cognitive plus postural task versus only postural task) and visual conditions (e.g. eyes open versus eyes closed).

Although the effects of acute total sleep deprivation [167–176], chronic low sleep quality [178] and social jetlag [179] on postural control had been previously

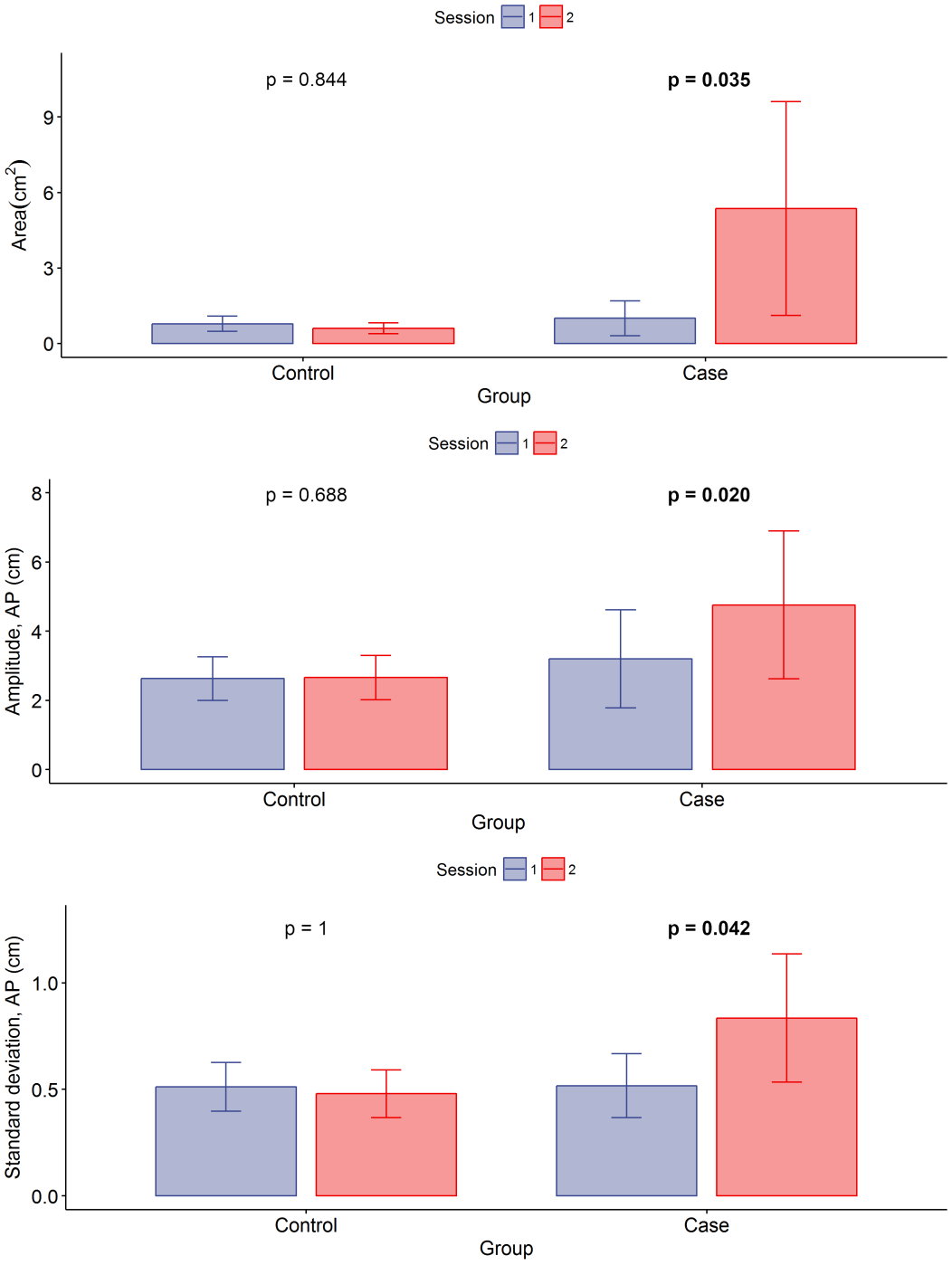

Figure 5.7: Centre of pressure displacement measures. Mean (bars) and standard error of the mean (error lines) by group and session. The *Control group* comprises subjects without day-to-day variations in sleep quality; the *Case group* comprises subjects with variations. *AP* anterior-posterior, *p* p-value from two-tailed paired Wilcoxon tests

investigated, the novelty of this study is that it focused on whether or not spontaneous variations in sleep quantity and quality over two consecutive nights may affect static balance. The findings suggest that a deterioration in sleep quantity and quality over two consecutive nights is associated with balance during unperturbed standing characterised by the centre of pressure displacement.

This finding may be relevant in the context of fall prevention, as previous studies have found significant associations between CoP displacement measures and risk of falling (although a consensus has not yet been reached on what are the key balance outcome measures for fall prediction) [10, 92, 200, 201]. Importantly, the findings presented in this chapter are based on the analysis of a small sample of young adults. Therefore, further research is required to confirm them in a larger sample of older adults.

An additional limitation of the present study relates to the fact that only two consecutive nights of sleep monitoring were considered. Further studies should consider a longer period (i.e. one week) in order to investigate longitudinal associations between sleep and balance.

5.6 Conclusions

This chapter presented a study performed to investigate the potential use of wearable devices for monitoring day-to-day variations in sleep quantity and quality, as well as the sensitivity of the balance control system to these variations.

Firstly, the results of this study suggest that wearable devices can be used for detecting day-to-day variations in sleep quantity and quality. In particular, the duration of rest periods and the presence of sleep disturbances can be estimated from acceleration and electrocardiogram signals.

Moreover, the results of the study suggest that day-to-day variations in sleep quantity and quality affect balance control during unperturbed standing. This situation can potentially expand the prevailing paradigm in fall prevention, from the current one focusing on the occasional assessment of risk factors and changes in the balance control system to a new one including also the continuous monitoring and detection of short-lived factors that might result in an imminent fall.

This study investigated the associations between day-to-day variations in sleep quantity and quality, monitored using wearable devices, and balance in unperturbed standing, thus answering the third research question underlying this thesis (see chapter 1). The study presented in the next chapter investigates whether quantitative descriptors of nonlinear dynamics are more sensitive than linear measures

to differences in balance control due to day-to-day variations in sleep quantity and quality. Hence, the study addresses the fourth research question.

Chapter 6

Day-to-Day Variations in Sleep Quality and Balance in Standing: the Role of Nonlinear Signal Analysis

6.1 Chapter overview

This chapter presents a study performed to investigate further the associations between day-to-day variations in sleep and balance observed in the previous study (chapter 5). Additionally, this study investigated whether nonlinear measures, especially Sample Entropy (SampEn), are sensitive to the differences in balance control produced by day-to-day variations in sleep quantity and quality.

6.2 Introduction

The study presented in chapter 5 investigated the potential use of wearable devices for monitoring day-to-day variations in sleep quantity and quality, as well as the sensitivity of the balance control system to these variations. The results suggested that wearable devices can be used for detecting day-to-day variations in sleep quantity and quality. Moreover, the results of that study also suggest that these variations in sleep affect balance control during unperturbed standing.

Moreover, the study presented in chapter 4 compared the sensitivity of linear and nonlinear measures to differences in balance control due to ageing and fall risk. The results of the study suggested that measures of nonlinear dynamics can reveal

differences in balance control that linear measures do not reveal.

This chapter presents a study performed to confirm and extend the findings of the studies mentioned earlier. Namely, the present study investigated further the associations between day-to-day variations in sleep and balance. As in the previous study (chapter 5), wearable devices were used for in-home sleep monitoring in order to confirm their potential use for capturing daily variations in sleep quantity and quality. Moreover, the study investigated further the association of those variations in sleep with variations in balance control. In contrast with the previous study, the present study explored the sensitivity of SampEn to the differences in balance control produced by day-to-day variations in sleep quantity and quality, based on the findings presented in chapter 4. Some preliminary results of this study were presented elsewhere [202].

6.3 Materials and methods

6.3.1 Study participants

Participants were recruited using e-mail advertising sent to postgraduate students from the School of Engineering, University of Warwick. Exclusion criteria included to have a medical history of sleep disorders, neurological or physical disabilities and to be in a pharmacological treatment potentially affecting sleep patterns and postural control (e.g. anti-depressants, hypnotics and stimulants).

Baseline characteristics, such as age, height, weight, general health status and use of medications, were collected during a baseline assessment and briefing session. All subjects provided informed consent before participating in the study. The research protocol was approved by the Biomedical and Scientific Research Ethics Committee of the University of Warwick (REGO-2014-1039 AM02).

6.3.2 Equipment

Sleep monitoring was performed using the Zephyr BioHarness 3.0 (Medtronic, Inc., Annapolis, MD, USA), a wearable device that measures and records tri-axial trunk acceleration and one-lead Electrocardiogram (ECG) signals at a sampling frequency of 100 Hz and 1 kHz, respectively, at a resolution of 12 bits per sample (Figure 6.1). The device is attached to chest over the xiphoid process (i.e. the bone structure located at the centre to the chest, below the lower part of the sternum) using a pair of pre-gelled, disposable electrodes. The device uses proprietary algorithms to calculate the user's activity level and posture based on the acceleration signals.

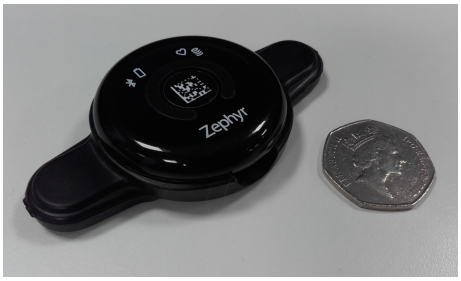

Figure 6.1: Wearable device used for sleep monitoring

Activity level is expressed in gravitational force units (i.e. g-force or simply g, where 1 g = 9.806 m/s^2) with a range from 0 to 16 g and is computed a

$$Activity = \sqrt{x^2 + y^2 + z^2} \tag{6.1}$$

where x, y and z are the average acceleration for the vertical, medial-lateral and anterior-posterior axes, respectively, over 1-second, non-overlapping windows. Posture is the wearer's angle of deviation from the vertical axis, where 0°=subject vertical, 90°=subject prone (face down) and -90°=subject supine (face up). Activity level and Posture time-series are reported with a frequency of 1 sample per second. Moreover, this device performs R peak detection on the ECG waveform and reports R-R intervals in milliseconds. Raw three-axial accelerations, ECG signals, R-R interval time-series, and a summary file containing the activity and posture time-series are stored in the internal memory of the device during use and can be downloaded for further processing. The validity and reliability of the Zephyr BioHarness are strong to very strong for heart rate, acceleration and posture monitoring at low to moderate physical activity levels [181, 182]. Figure 6.2 shows representative activity and posture signals during sleep.

Balance testing was performed using a tri-axial force platform (Advanced Mechanical Technology, Inc., Watertown, MA, USA) at a sampling frequency of 1 kHz. Based on force data, the Vicon Nexus 1.4.116 software (Vicon Motion Systems Ltd., Oxford, UK) computes the net Centre of Pressure (CoP) location for each frame. CoP displacement is stored as time-series of numerical data in the Anterior-Posterior (AP) and Medial-Lateral (ML) axes in relation to the orientation of the subject orientation. Figure 6.3 shows a participant standing quietly on the force plate and the corresponding CoP displacement trajectory.

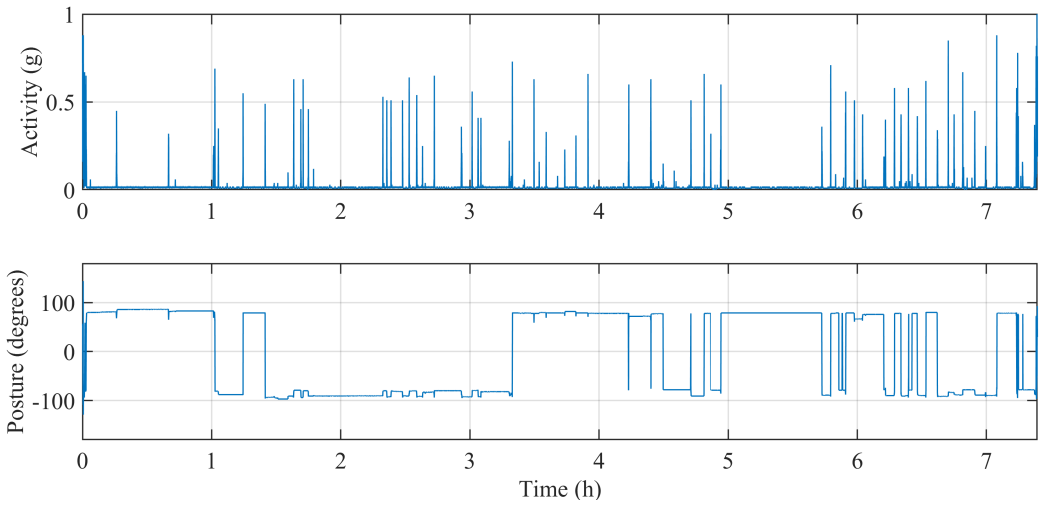

Figure 6.2: Activity (top) and posture (bottom) signals during sleep for a participant who reported very poor sleep quality. Activity level is expressed in gravitational force units with a range from 0 to 16 g (1 g = 9.806 m/s^2). Posture is the wearer's angle of deviation from the vertical axis, where 0°=subject vertical, 90°=subject prone (face down) and -90°=subject supine (face up). Data collected by the author as part of this study.

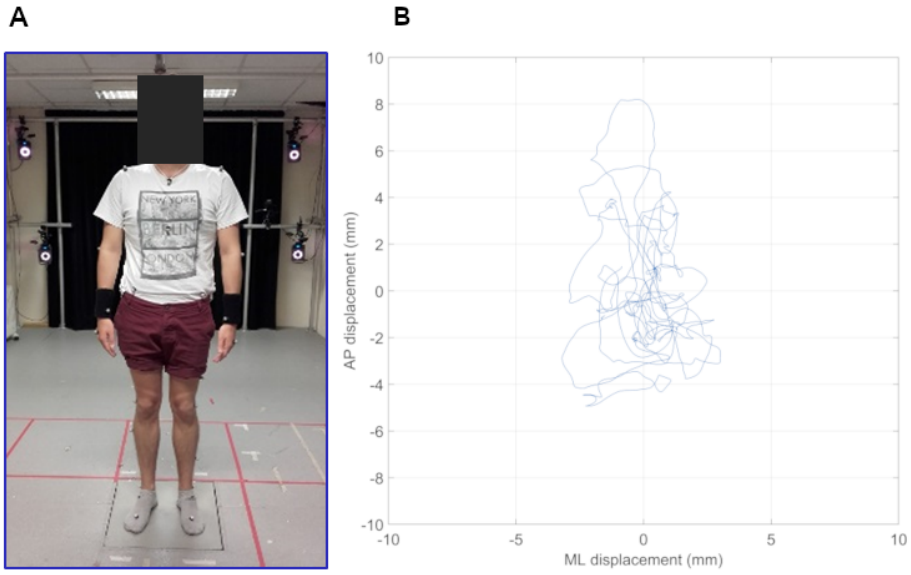

Figure 6.3: Balance assessment: **(A)** Participant standing quietly on the force plate and **(B)** Centre of pressure trajectory. *AP* anterior-posterior, *ML* medial-lateral. Data collected by the author as part of this study.

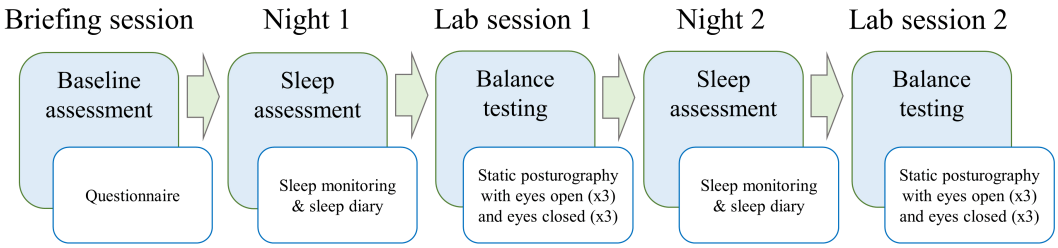

Figure 6.4: Schematic diagram of the study protocol. Sleep monitoring was performed using a wearable patch-type device that records acceleration and electrocardiogram signals. Balance testing was performed using static posturography.

6.3.3 Study protocol

A schematic of the study protocol is shown in Figure 6.4. After baseline assessment, participants underwent sleep and balance assessment for two consecutive days. For sleep assessment, they were asked to wear the BioHarness during sleep; i.e., to apply it at the time of usual bedtime and to take it off after the final awakening. Additionally, subjects were required to complete the Consensus Sleep Diary (CSD) every morning immediately after getting out of bed during their participation in the study [31]. Participants were invited to stick to their regular sleep schedule and habits (i.e. no intervention was applied).

Balance was assessed in two morning sessions starting at the same time of the day (9:00 or 10:00 a.m.) for any given participant. Previous studies have suggested that CoP measures change throughout the day, allegedly following a circadian pattern [168–170]. By starting both sessions at the same time of the day, the influence of time of day on postural control measures was discarded as a potential confounder. At each session, participants were asked to complete six quiet standing trials, three with Eyes Open (EO) and three with Eyes Closed (EC). For the EO trials, they were instructed to stand quietly on the force platform placing the feet in a comfortable position (about shoulder width), letting the arms hang naturally at their sides and stare at a point on the wall in front of them. For the EC, subjects were instructed to close their eyes once they had stepped on the force plate, set the feet in a comfortable position, and leave their arms to hang naturally. The duration of each recording was 30 seconds and a brief resting interval (≈15 seconds) was allowed between trials. Participants wore socks but no shoes during data acquisition, in order to discard spurious differences in balance due to footware (e.g. additional support and altered foot sole sensation) [188, 203].

6.3.4 Data processing

Data collected via the sleep diary, the BioHarness and the force platform were processed as described in the following subsections in order to compute a set of sleep and balance measures. A summary of those measures is shown in Table 6.1.

6.3.4.1 Sleep diary measures

Five sleep measures were extracted from the sleep diary (Table 6.1): 1) Sleep Onset Latency (SOL); 2) Wake After Sleep Onset (WASO), a measure of sleep fragmentation; 3) Total Sleep Time (TST) or sleep duration; 4) Sleep Efficiency (SE), and; 5) Subjective Sleep Quality (SSQ).

6.3.4.2 Sleep activity level measures

Activity level signals were processed to compute six measures of activity during sleep (Figure 6.5). Firstly, raw signals were trimmed based on posture data to discard activity data outside the sleep period (i.e. before getting into and after getting out of bed). Then, the signals were segmented into continuous, non-overlapping 1-minute epochs and activity counts were computed for each epoch using the zero-crossing mode, described in section 2.5; i.e., the activity level was compared with the reference activity level, and each threshold crossing generated an activity count [124]. The threshold was set to 0.1 g for high sensitivity. This generated a time-series $\langle ACT(n) \rangle$ with the form

$$\langle ACT(n) \rangle = ACT(1), ACT(2), \ldots, ACT(N)$$

where $ACT(i)$ is the number of activity counts for the 1-minute i^{th} 1-minute epoch and N is the total number of 1-minute epochs.

Subsequently, an *inactive interval* was defined as a sequence of two or more consecutive epochs whose number of activity counts is equal to zero. Based on this definition, the $\langle ACT(n) \rangle$ was examined to determine the number and duration of inactive intervals, which produced a time-series $\langle I(m) \rangle$ of the form

$$\langle I(m) \rangle = I(1), I(2), \ldots, I(M)$$

where $I(j)$ is the duration (minutes) of the j^{th} inactive interval and M is the total number of inactive intervals.

Finally, six activity measures were computed as described in chapter 5 (equations 5.3.4.2 to 5.7). These measures were computed using in-house written scripts

in MATLAB R2017b (The Mathworks, Inc., Natick, MA, USA). The source code can be found in Appendix A.

6.3.4.3 Heart rate variability measures

Heart Rate Variability (HRV) measures were computed from R-R interval time-series in order to characterise autonomic cardiac modulation during sleep (Figure 6.5). A higher parasympathetic tone has been observed during Non-Rapid Eye Movement (NREM), particularly during deep sleep; in contrast, a higher sympathetic tone has been observed during wake intervals, Rapid Eye Movement (REM) and sleep arousals [35]. Therefore, the HRV analysis provided with an indication of the presence of wake intervals and arousals, as well as of shorter deep sleep periods.

Firstly, the R-R series were segmented based on posture data to discard heartbeats outside the sleep period. Subsequently, the software HRVanalysis was used to correct R-R time-series and compute four HRV measures from them: two frequency-domain measures (Low-Frequency (LF) and High-Frequency (HF) power) and two nonlinear measures (Approximate Entropy (ApEn) and SampEn) [186]. The automatic R-R interval correction algorithms involve two steps. First, spurious R-R intervals are detected based on the relative variation in successive intervals: R-R intervals with a variation of +32.5% or -24.5% are considered to be spurious and thus discarded [187]. Second, discarded R-R intervals are recalculated as follows: if the number of successive false R-R intervals is 3 or less, these are recalculated by cubic spline interpolation; otherwise, they are replaced by copying the same number of previous valid R-R intervals [186]. In addition, three frequency-domain measures were computed in MATLAB R2017b: LF normalised, HF normalised and LF/HF ratio. The meaning of these HRV measures has been widely described in literature [126, 127]. In the context of sleep assessment, those features are associated with specific sleep stages and other relevant phenomena (e.g. arousals) [126]. In the frequency-domain, HF power describes the parasympathetic activity, whereas LF power describes both parasympathetic and sympathetic activity. Thus, the relationship between both branches usually is explored with the normalised frequency values and the LF/HF ratio. A higher LF/HF ratio reflects a higher HRV. Finally, entropy measures represent an index of regularity in the cardiac signal. An increase in regularity (i.e., an increase in the entropy measure) is associated with parasympathetic modulation, and its decrease is interpreted as the result of an increased sympathetic tone.

Table 6.1: Summary of sleep and balance measures

Measure	Units	Description
Sleep measures		
Sleep diary measures		
Sleep onset latency (SOL)	minutes	Duration of the transition interval from wakefulness to sleep. It is a measure of sleep fragmentation
Wake after sleep onset (WASO)	minutes	Total duration of intervals of wakefulness between sleep onset and final awakening
Total sleep time (TST)	h	Total duration of actual sleep
Sleep efficiency (SE)	%	Ratio of total sleep time to time-in-bed expressed as a percentage
Subjective sleep quality (SSQ)	-	Subjective appraisal of quality of sleep (1=Very poor, 2=Poor, 3=Fair, 4=Good, 5=Very good)
Activity level measures		
ACT_{mean}	counts	Mean activity counts per epoch over the entire sleep opportunity
ACT_{sd}	counts	Standard deviation of activity counts per epoch over the entire sleep opportunity
Activity Index (AI)	%	Percentage of 1-minute epochs with activity counts >0
Fragmentation Index (FI)	%	Percentage of inactive intervals with duration $\leq$ 5 minutes
I_{max}	minutes	Duration of the longest inactive interval
I_{mean}	minutes	Average duration of all inactive intervals

Table 6.1 continued from previous page

Measure	Units	Description
HRV measures		
LF	ms^2	Power in the low-frequency range (0.04-0.15 Hz)
HF	ms^2	Power in the high-frequency range (0.15-0.4 Hz)
LF normalised	-	LF power in normalised units computed as LF / LF+HF x 100
HF normalised	-	HF power in normalised units computed as HF / LF+HF x 100
LF/HF ratio	-	Ratio LF to HF
Approximate entropy (ApEn)	-	A measure of the regularity or predictability of fluctuations in the R-R time-series
Sample entropy (SampEn)	-	A modification of ApEn that reduces the chances to overestimate the entropy in a time-series
Balance measures		
Total length	mm	Length of the CoP trajectory on the base of support
Standard deviation	mm	Dispersion of the CoP position around the mean
Amplitude	mm	Distance between the minimum and maximum positions. Also known as *range*.
Total mean velocity	mm/s	Mean velocity of the CoP motion on both directions (i.e. AP and ML)
Mean velocity	mm/s	Mean velocity of the CoP motion for each direction (i.e. AP/ML)
Area	mm^2	Area of the ellipse that contains 95% of the CoP points
Sample entropy (SampEn)	-	Regularity or predictability of the CoP time-series

HRV heart rate variability, *CoP* centre of pressure, *AP* anterior-posterior, *ML* medial-lateral

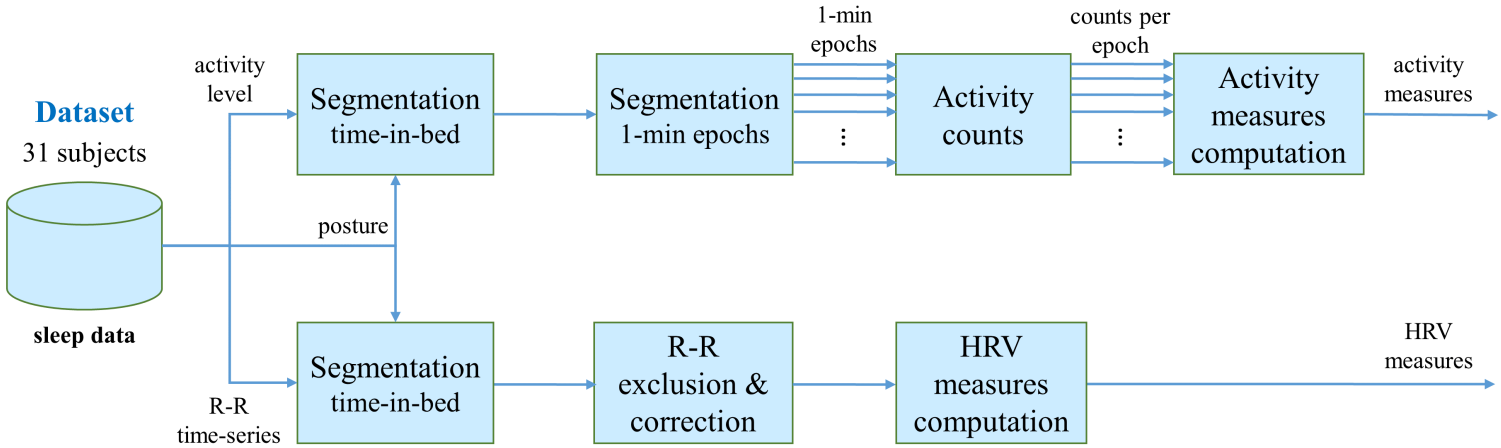

Figure 6.5: Block diagram of sleep data processing. Activity level time-series were trimmed based on posture data to discard intervals outside the sleep period. Then, the time-series were segmented in continuous, non-overlapping 1-minute epochs and activity counts were computed for each epoch. Finally, six measures of activity were computed for each epoch. R-R time-series were also trimmed based on posture data. Then, seven heart rate variability measures were computed in order to characterise autonomic cardiac modulation during sleep.

6.3.4.4 Balance measures

A block diagram depicting the steps followed for CoP data processing is shown in Figure 6.6. Firstly, CoP time-series were passed through a fourth-order zero-phase Butterworth low-pass digital filter with a cut-off frequency of 10 Hz in order to replicate the initial specifications of CoP time-series used in the study described in chapter 4. Then, the resulting signals were processed differently as required for the computation of CoP linear measures and sample entropy.

Linear measures. CoP time-series were downsampled by a factor of 10 to achieve an effective sampling frequency of 100 Hz. Subsequently, the CoP time-series were detrended (i.e., subtraction of the mean value from the time-series). Finally, six CoP displacement linear measures were computed as described in section 2.4: Amplitude, Standard deviation, Mean velocity, Total length, Total mean velocity and Area. Amplitude, Standard deviation and Mean velocity were computed independently for the AP and the ML axes, producing a value for each displacement direction. By definition, Total length, Total mean velocity and Area are composite measures of displacement that consider the CoP displacement in both directions.

Sample entropy. CoP time-series were downsampled by a factor of 50 to achieve an effective sampling frequency of 20 Hz, thus replicating the specifications of the time-series in the study described in chapter 4. Then, SampEn was computed using $m = 5$, $r = 0.1$ and $N = 600$ data points (20 Hz x 30 s).

Scripts for CoP data processing were also written in MATLAB R2017b. The source code can be found in Appendix A.

6.3.5 Statistical analysis

Participants were grouped according to the sleep quality scores they reported in the sleep diary (SSQ). Those who reported no variation in sleep quality over two consecutive nights were assigned to the *Control group*. Participants who reported a variation in sleep quality over two consecutive nights (e.g. good sleep quality in one night and poor sleep quality in the other) were assigned to the *Case group*. The validity of self-reported sleep quality was tested by running pairwise comparisons for all other sleep measures within each group. By definition, no differences over consecutive nights were expected for the *Control group*, while significant differences were expected for the *Case group*. Two-sided Wilcoxon paired tests with a significance level set at 0.05 were used for these comparisons, given that most sleep measures exhibited a non-normal distribution (Shapiro-Wilk test with a p-value < 0.05).

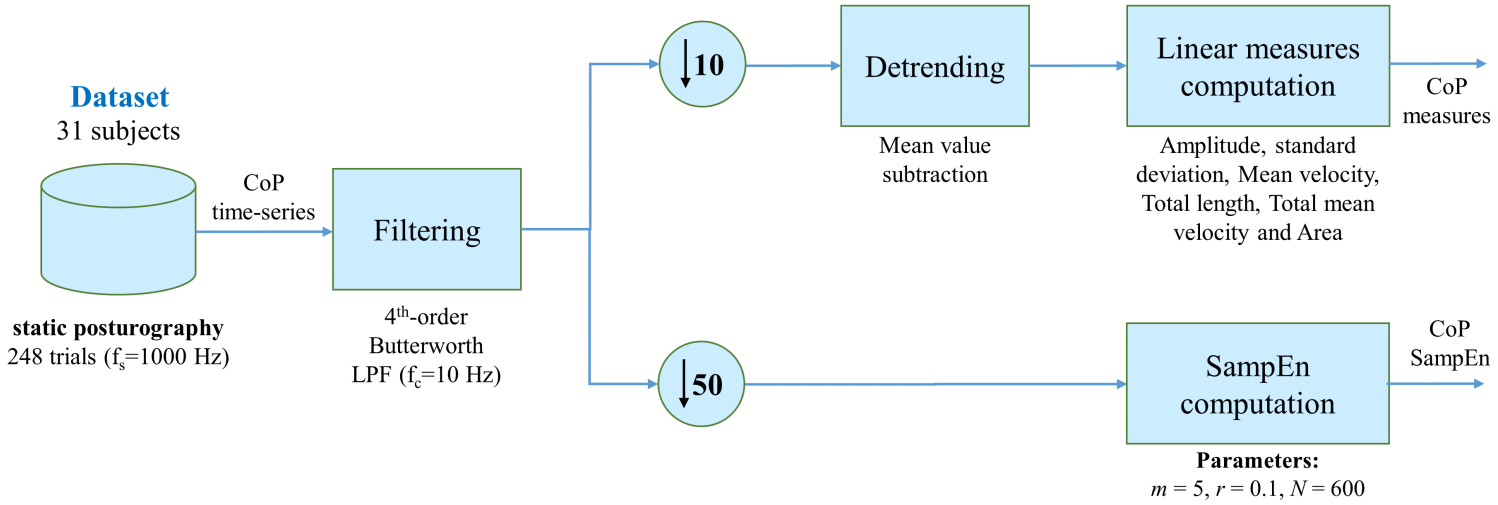

Figure 6.6: Block diagram of centre of pressure (CoP) data processing. Raw CoP signals were filtered to remove acquisition noise. Six linear measures were computed, after downsampling (factor=10) and detrending the filtered CoP time-series. Sample entropy was computed for $m = 5$, $r = 0.1$ and $N = 600$, after downsampling the filtered CoP time-series by a factor of 50.

Subsequently, a repeated measures Analysis of Variance (ANOVA)-type rank test for factorial designs was performed in order to test the main effects and the interaction effects of *Group* and *Session* on balance measures [190]. This test was developed for experimental designs where subjects are stratified in several groups, as well as observed at different time points (i.e., mixed designs). Importantly, these tests are robust to outliers and small sample sizes. The computational implementation of this test provided by the authors through the R package nparLD version 2.1 was used [191]. The main effects and interaction effects of *Group* and *Session* were tested for the CoP linear measures and SampEn. A p-value < 0.05 was accepted as indicative of statistical significance. This analysis was performed in R version 3.4.1 (R Foundation for Statistical Computing, Vienna, Austria).

Finally, differences in CoP linear measures and SampEn between sessions were investigated for each group: for the *Control group*, pairwise comparisons were always made between Session 2 and Session 1, given that by definition for this group sleep quality was equally rated in both sleep opportunities; for the *Case group*, pairwise comparisons were made between the session with the poorest sleep quality and the session with the best sleep quality, regardless of the chronological order in which they were presented. Two-tailed Wilcoxon paired tests were performed given the non-normal distribution of most balance measures (Shapiro-Wilk test with a p-value < 0.05). A p-value < 0.05 was accepted as indicative of statistical significance. These tests were conducted in MATLAB R2017b.

6.4 Results

6.4.1 Participants baseline characteristics and stratification

Thirty-one healthy volunteers (14 females and 17 males) participated in this study, from which seven also participated in the study reported in chapter 5. The sample had an overall mean (standard deviation) age of 28.8 (4.7) years, height of 172.1 (10.6) cm, mass of 72.3 (14.8) kg and body mass index of 24.2 (3.2) kg/m^2. No significant differences were found between groups for these characteristics (Table 6.2).

Seven participants reported no variation in sleep quality over two consecutive nights (*Control group*), whereas 24 participants reported a variation in sleep quality over two consecutive nights (*Case group*). No significant differences were found in sleep measures over the two consecutive nights for the *Control group*. Conversely, the *Case group* exhibited significant differences for some sleep measures (Table 6.3). Namely, for the poorest sleep quality night (i.e., the lowest-rated) the *Case group*

Table 6.2: Baseline characteristics of study participants. Mean and standard deviation for all subjects, subjects without day-to-day variation in sleep quality (*Control group*) and subjects with variation in day-to-day sleep quality (*Case group*).

	All (n = 31)		Control group (n = 7)		Case group (n = 24)		
Variable	Mean	SD	Mean	SD	Mean	SD	p
Age (years)	28.8	4.7	29.7	5.2	28.5	4.6	0.557
Mass (kg)	72.3	14.8	69.3	16.3	73.2	14.6	0.551
Height (cm)	172.1	10.6	169.9	12.3	172.8	10.2	0.534
BMI (kg/m^2)	24.2	3.2	23.7	3.5	24.3	3.1	0.678

SD standard deviation, *BMI* body mass index, *p* p-values from two-tailed paired t-tests

exhibited:

- Longer WASO (p=0.004), shorter TST (p<0.001) and lower SE (p=0.039), as self-reported in the sleep diary.
- Shorter mean duration of the longest inactive interval (p=0.016), as computed from the trunk acceleration signals.
- Lower heart rate variability, as reflected by a lower power in the HF band (p=0.007) and lower ApEn and SampEn (p=0.020 and p=0.036, respectively).

6.4.2 Group and Session main effects and interaction effects on balance measures

6.4.2.1 Linear measures

The main effects of *Session* were found significant for one CoP displacement measure under the EC testing condition Table 6.4.

No significant *Group*Session* interactions were found for CoP displacement measures under the EO testing condition. Conversely, two CoP displacement linear measures showed significant *Group*Session* interaction effects under the EC testing condition:

- Standard deviation in the ML direction (p=0.044)
- Mean velocity in the ML direction (p=0.037)

6.4.2.2 Sample entropy

Neither main nor interaction effects were found significant for CoP sample entropy (Table 6.5).

Table 6.3: Day-to-day differences in sleep measures. Median difference and interquartile range of the median difference subjects without day-to-day variation in sleep quality (*Control group*) and subjects with variation in day-to-day sleep quality (*Case group*).

	Control group (n = 7)			Case group (n = 24)			
Measure	Median	IQR	p	Median	IQR	p	Trend
Sleep diary measures							
SOL (min)	0	14.375	0.563	0	15	0.721	-
WASO (min)	1	2.750	0.219	10	33.5	**0.004**	↑↑
TST (h)	0.75	0.813	0.313	-1	1.34	**<0.001**	↓↓
SE (%)	1	5	0.454	-7.5	13	**0.039**	↓↓
Activity level measures							
ACT_{mean} (counts)	-0.027	0.066	0.469	0.014	0.173	0.306	↑
ACT_{sd} (counts)	-0.097	0.124	0.078	0.035	0.469	0.485	↑
Activity Index (%)	0.269	2.231	0.469	0.573	3.894	0.211	↑
Fragmentation Index (%)	-0.690	10.430	0.469	3.675	20.021	0.095	↑
I_{max} (min)	-5	24	0.500	-9.5	21	**0.016**	↓↓
I_{mean} (min)	-2.410	8.304	0.219	-2.086	7.482	0.067	↓
HRV measures							
LF (ms^2)	-88.286	282.537	0.563	-206.165	444.057	0.050	↓
HF (ms^2)	-66.471	77.059	0.438	-77.199	196.967	**0.007**	↓↓
LF normalised	0.517	6.023	0.844	0.420	6.835	0.306	↑
HF normalised	-0.517	6.023	0.844	-0.420	6.835	0.306	↓
LF/HF ratio	0.145	1.476	1	0.122	0.920	0.372	↑
ApEn	0.001	0.047	0.987	-0.032	0.072	**0.020**	↓↓
SampEn	0.008	0.079	0.871	-0.027	0.093	**0.036**	↓↓

MD median difference, *IQR* interquartile range, *p* p-values from two-tailed paired Wilcoxon tests, *SOL* sleep onset latency, *WASO* wake after sleep onset, *TST* total sleep time, *SE* sleep efficiency, *HRV* heart rate variability, *LF* low-frequency power, *HF* high-frequency power, *ApEn* approximate entropy, *SampEn* sample entropy
Bold values indicate significant differences
↓↓ (↑↑): significantly lower (higher) for poorer sleep quality night
↓ (↑): lower (higher) for poorer sleep quality night

6.4.3 Pairwise comparisons for balance measures

6.4.3.1 Linear measures

No significant differences in linear measures were observed for CoP displacements under the EO testing condition, neither for subjects in the *Control group* nor for those in the *Case group*. As for CoP displacements in the EC testing condition, three linear measures exhibited significant differences after sleep deterioration (*Case group*) (Table 6.6). Namely, after the lowest-rated sleep participants showed a stiffer balance control as reflected by:

- a decrease in the total length of displacement (p=0.012)
- a decrease in the total mean velocity of displacement and mean velocity in the ML direction (p=0.012 and p=0.013, respectively)

Conversely, no significant CoP displacement measure variations were observed in the *Control group* (i.e., subjects presenting no sleep quality variations) under the EC testing condition.

6.4.3.2 Sample entropy

No significant differences in CoP sample entropy were observed under the EO testing condition, neither for participants in the *Control group* nor for those in the *Case group*. Under the EC testing condition, participants in the (*Case group*) showed a significantly lower CoP sample entropy (Table 6.7).

Table 6.4: Main effects and interactions effects of *Group* and *Session* on centre of pressure linear measures.

Factor / Interaction	Group		Session		Group*Session	
Measure	Fn	p	Fn	p	Fn	p
Eyes open						
Total length	0.246	0.620	0.081	0.776	2.031	0.154
Standard deviation, AP	0.070	0.791	0.140	0.709	0.186	0.666
Standard deviation, ML	0.449	0.503	0.781	0.377	0.388	0.533
Amplitude, AP	0.071	0.790	0.455	0.500	0.045	0.831
Amplitude, ML	0.128	0.720	0.063	0.802	0.042	0.838
Total mean velocity	0.246	0.620	0.081	0.776	2.031	0.154
Mean velocity, AP	0.742	0.389	0.057	0.811	1.410	0.235
Mean velocity, ML	0.021	0.885	0.163	0.686	2.341	0.126
Area	0.113	0.736	0.500	0.479	0.799	0.371
Eyes closed						
Total length	2.011	0.156	0.758	0.384	3.775	0.052
Standard deviation, AP	0.088	0.767	1.867	0.172	0.867	0.352
Standard deviation, ML	1.252	0.263	1.875	0.171	4.074	**0.044**
Amplitude, AP	1.320	0.251	0.142	0.706	0.003	0.954
Amplitude, ML	1.537	0.215	1.165	0.280	2.603	0.107
Total mean velocity	2.011	0.156	0.758	0.384	3.775	0.052
Mean velocity, AP	2.112	0.146	0.313	0.576	2.710	0.100
Mean velocity, ML	0.834	0.361	0	0.996	4.360	**0.037**
Area	0.666	0.415	3.902	**0.048**	3.712	0.054

AP anterior-posterior, *ML* medial-lateral, *Fn* ANOVA-type statistic, *p* p-values from ANOVA-type non-parametric two-tailed paired tests.
Bold values indicate significant interactions

Table 6.5: Main effects and interactions effects of *Group* and *Session* on centre of pressure sample entropy.

Factor / Interaction	Group		Session		Group*Session	
Measure	Fn	p	Fn	p	Fn	p
Eyes open	3.623	0.057	0	0.986	0.119	0.730
SampEn, AP	0.114	0.736	0.984	0.321	0.004	0.952
SampEn, ML						
Eyes closed						
SampEn, AP	1.942	0.163	0.447	0.504	0.820	0.365
SampEn, ML	0.381	0.537	0.529	0.467	0.033	0.856

SampEn sample entropy, *AP* anterior-posterior, *ML* medial-lateral, *Fn* ANOVA-type statistic, *p* p-values from ANOVA-type non-parametric two-tailed paired tests.

Table 6.6: Day-to-day differences in centre of pressure displacement linear measures. Median difference and its interquartile range for subjects without day-to-day variation in sleep quality (*Control group*) and subjects with variation in day-to-day sleep quality (*Case group*).

	Control group (n = 7)			Case group (n = 24)			
Measure	MD	IQR	p	MD	IQR	p	Trend
Eyes open							
Total length (mm)	13.350	63.294	0.188	-6.655	82.352	0.638	↓
Standard deviation, AP (mm)	0.786	2.757	0.438	-0.145	2.116	0.661	↓
Standard deviation, ML (mm)	0.575	1.199	0.438	0.058	1.425	0.592	↑
Amplitude, AP (mm)	1.740	17.423	0.625	0.210	8.851	0.685	↑
Amplitude, ML (mm)	1.602	5.334	0.625	1.033	6.641	0.338	↑
Total mean velocity (mm/s)	0.445	2.110	0.188	-0.222	2.745	0.638	↓
Mean velocity, AP (mm/s)	0.163	1.778	0.313	0.010	1.976	0.615	↑
Mean velocity, ML (mm/s)	0.170	0.973	0.309	-0.144	1.352	0.912	↓
Area (mm^2)	42.187	199.847	0.438	0.488	58.804	0.858	↑
Eyes closed							
Total length (mm)	2.698	61.867	0.625	-23.728	65.311	**0.012**	↓↓
Standard deviation, AP (mm)	0.009	2.341	0.625	-0.021	1.310	0.661	↓
Standard deviation, ML (mm)	0.788	1.192	0.313	-0.259	1.188	0.291	↓
Amplitude, AP (mm)	-1.647	8.623	0.813	-0.085	5.68	0.961	↓
Amplitude, ML (mm)	1.242	6.489	0.438	-1.308	5.481	0.548	↓
Total mean velocity (mm/s)	0.090	2.062	0.625	-0.791	2.177	**0.012**	↓↓
Mean velocity, AP (mm/s)	0.200	1.333	0.438	-0.296	1.581	0.088	↓
Mean velocity, ML (mm/s)	0.198	1.462	0.438	-0.493	1.451	**0.013**	↓↓
Area (mm^2)	63.180	178.142	0.125	-8.795	169.573	0.372	↓

AP anterior-posterior, *ML* medial-lateral, *MD* median difference, *IQR* interquartile range, *p* p-values from two-tailed paired Wilcoxon tests

Bold values indicate significant differences

↓↓ (↑↑): significantly lower (higher) for poorer sleep quality night

↓ (↑): lower (higher) for poorer sleep quality night

Table 6.7: Day-to-day differences in centre of pressure displacement sample entropy. Median difference and its interquartile range for subjects without day-to-day variation in sleep quality (*Control group*) and subjects with variation in day-to-day sleep quality (*Case group*).

	Control group (n = 7)			Case group (n = 24)			
Measure	MD	IQR	p	MD	IQR	p	Trend
Eyes open							
SampEn, AP	-0.038	0.137	0.813	0.001	0.139	0.733	↑
SampEn, ML	-0.047	0.257	0.813	-0.018	0.127	0.249	↓
Eyes closed							
SampEn, AP	0.008	0.133	1	-0.033	0.139	0.131	↓
SampEn, ML	-0.081	0.236	0.813	-0.029	0.057	**0.042**	↓↓

SampEn sample entropy, *AP* anterior-posterior, *ML* medial-lateral, *MD* median difference, *IQR* interquartile range, *p* p-values from two-tailed paired Wilcoxon tests
Bold values indicate significant differences
↓↓: significantly lower or poorer sleep quality night
↓: lower for poorer sleep quality night

6.5 Discussion

This study was based on the findings presented in chapters 4 and 5. Firstly, the study aimed to investigate further whether day-to-day self-reported sleep quality was confirmed by instrumented sleep assessment. Therefore, participants were divided into two groups based on whether or not they reported a shift in sleep quality over two consecutive nights. As in the previous study, reported changes in sleep quality were not artificially induced; they were instead the consequence of natural sleep disturbances experienced during the lowest-rated sleep opportunity (e.g. the need to use the toilet and an uncomfortable room temperature). Subjects reporting a shift in sleep quality reported significantly higher sleep fragmentation (WASO), shorter sleep duration (TST) and lower sleep efficiency (SE) for the lowest-rated sleep period. They also showed shorter inactive intervals measured from body acceleration signals, suggesting a less quiet and more fragmented sleep. Moreover, subjects reporting a variation in sleep quality also exhibited higher sympathetic activity (i.e., lower heart rate variability) during the lowest-rated sleep opportunity, which suggests the presence of more wake intervals and arousals, as well as fewer and shorter deep sleep intervals [35]. Generally speaking, these results are in agreement with those reported in chapter 5. Moreover, these results confirmed that wearable devices could be used to detect day-to-day variations in sleep quantity and quality.

The interaction effects of *Group* and *Session* on balance measures were tested. Two CoP displacement linear measures showed significant *Group*Session* interactions (Table 6.4), suggesting that day-to-day variations in balance are asso-

ciated with variations in sleep quantity and quality over consecutive nights.

The *Group*Session* interaction effects above were found to be attributable to subjects that exhibited a variation in sleep quantity and quality over consecutive nights. The group of subjects reporting and exhibiting worsening in sleep over two consecutive days exhibited shorter, slower and more regular CoP displacements under the EC testing condition, particularly in the ML axis. In contrast with the results obtained in the previous study, no significant differences were observed for any CoP measure in the AP axis under the EO condition. Nevertheless, shorter and slower CoP motion in the ML direction has been observed in healthy subjects tested under high cognitive load conditions (e.g. dual-task) [175]. Also, more regular ML CoP time-series were observed for older adults at higher risk of falling in the study presented in chapter 4 [153].

Altogether, the results from this study also suggest that a shorter and more fragmented sleep affects balance control in unperturbed standing.

6.6 Conclusions

This chapter presented a study performed to confirm and extend the findings of the studies mentioned earlier. Namely, this study investigated further the associations between day-to-day variations in sleep and balance. The results confirmed the potential of wearable devices for in-home sleep monitoring with the aim of capturing daily variations in sleep quantity and quality.

Moreover, the study investigated further the association of those variations in sleep with variations in balance control. Interestingly, both linear measures and SampEn were able to capture the differences in balance control resulting from day-to-day variations in sleep quantity and quality.

This study investigated whether quantitative descriptors of nonlinear dynamics are more sensitive than linear measures to differences in balance control due to day-to-day variations in sleep quantity and quality, thus addressing the fourth and final research question underlying this thesis (see chapter 1). The next chapter summarises the main conclusions of this research and provides some recommendations for further work based on the identified limitations and opportunities.

Chapter 7

Conclusions and Further Work

7.1 Chapter overview

This chapter presents the main conclusiond of this thesis. Section 7.2 restates the scope, aim and objectives of this work. Section 7.3 recapitulates the research gaps and questions that motivated this work and summarises the work done and the main findings. Section 7.4 provides recommendations for further work, based on the limitations and opportunities identified in this research. Section 7.5 presents some final remarks.

7.2 Scope, aim and objectives

The spread of wearable technology is empowering innovative ways of assessing balance and risk of falling in older adults. Wearable inertial sensors are a promising complement to clinical balance assessment tools since they potentially provide an objective and accurate quantification of the timing and kinematics of functional tasks.

Moreover, wearable devices also enable the ambulatory monitoring of physiological and behavioural variables, which can be used to infer health status and health-related behaviours linked to impaired balance and fall risk. This situation could conceivably enrich the prevailing paradigm in fall prevention, from the current one mainly involving the occasional assessment of risk factors to a novel paradigm also including the continuous monitoring and detection of short-lived factors that might result in an imminent fall.

Additionally, the diffusion of dynamical systems theory and methods within the medical research community are stirring a new approach to the study of ageing

and balance in older adults. In particular, nonlinear signal analysis methods could potentially provide further information on the underlying control mechanisms in ageing and produce more sensitive measures of fall risk.

Despite the advantages that this can provide, there are several challenges in the adoption of wearable technologies and nonlinear analysis methods for balance and fall risk assessment, which still preclude a firm conclusion on their scientific and clinical value. This research aimed to advance the knowledge and methods related to the use of wearable sensors and nonlinear signal analysis for the assessment of balance and fall risk, both in research and clinical settings and ambulatory monitoring of health status and behaviours linked to impaired balance.

Accordingly, the main objectives of this research were:

Objective 1: To identify the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults, including sensor placement, movement task and measured variable(s).

Objective 2: To determine whether quantitative descriptors of nonlinear dynamics are more sensitive than linear measures to differences in balance control due to ageing and fall risk.

Objective 3: To determine whether day-to-day variations in sleep quantity and quality, monitored using wearable devices, are associated with balance control variations.

Objective 4: To determine whether quantitative descriptors of nonlinear dynamics are more sensitive than linear measures to differences in balance control due to day-to-day variations in sleep quantity and quality

7.3 Research questions and answers

The objectives above were derived from a set of research questions identified through a review of the literature (chapter 2). These questions are restated below, each followed by the research gap on which it is based, a summary of the work carried out to address them and the main findings.

Research question 1: What is the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults, given the variety in sensor placements, movement tasks and measured variables that these devices allow?

In the last two decades, the use of wearable inertial sensors for fall risk assessment has been on the rise. Researchers have used these sensors with the aim of producing instrumented functional balance tests [10–12]. In their studies, subjects were asked to perform one or more movement tasks while wearing one or more inertial sensors on different body landmarks. Moreover, subjects at high risk of falling were identified based on retrospective fall history (i.e. self-reported previous falls), prospective fall occurrence, clinical assessment (e.g. Timed-Up-and-Go test (TUG test)) or a combination thereof. This information and the features extracted from the recorded signals were later used to develop mathematical or statistical models for predicting further fall occurrences or classifying subjects into fall risk categories. Some reviews on the topic have revealed a considerable heterogeneity between studies regarding the sensor placement, movement task, features and models used for the development of sensor-based fall risk assessment tools [10–12]. This heterogeneity hinders any firm conclusions on the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults [11, 12].

Chapter 3 presented an original systematic review and meta-analysis performed in order to identify the optimal wearable inertial sensor-based protocol for assessing fall risk in older adults, including sensor placement, movement task and measured variables (or features). A data set of 175 wearable inertial sensor-based features extracted from 13 studies was analysed in order to identify an optimal protocol. Namely, studies that used wearable inertial sensors for discriminating fallers from non-fallers were systematically reviewed. Standard methods for the analysis of categorical data were used to identify optimal combinations of sensor placement, movement task and features. Additionally, standard methods for the meta-analysis of continuous variables were used to identify significant features for discrimination between fallers and non-fallers.

The results of the analyses above suggest that the instrumented TUG test is a suitable tool for discriminating non-fallers and fallers, provided that the inertial sensors are placed on the shins and angular velocity, temporal (e.g. total time and step time) and spatial (e.g. number of steps) features are computed. Additionally, the evidence also suggests that an additional sensor placed on the lower back could potentially provide relevant measures derived from accelerations during sit-to-stand and stand-to-sit transitions. The study has been published elsewhere [128].

Research question 2: Are quantitative descriptors of nonlinear dynamics more sensitive than linear measures to differences in balance control due to ageing and fall risk? If so, what is the optimal way to apply them (e.g. signal pre-processing, selection of input parameters)?

The diffusion of nonlinear dynamical systems theory in the biomedical research community has inspired the use of quantitative descriptors of nonlinear dynamics for assessing balance control. In particular, Approximate Entropy (ApEn) and Sample Entropy (SampEn) have been proposed as a measure of body sway regularity during unperturbed standing. However, their ability to discriminate between groups with different fall risk and the suitable selection of the input parameters needed for their computation, have not yet been formally investigated.

Chapter 4 presented a study performed to investigate whether ApEn and SampEn are more sensitive than linear measures to differences in balance control due to ageing and fall risk, as well as to identify the optimal way to apply them (i.e. signal pre-processing and selection of input parameters). A public dataset of Centre of Pressure (CoP) time-series from 163 subjects was used [27]. Subjects were grouped into young adults (age<60, n=85), and older adults (age≥60) with (n=18) and without (n=56) falls in the previous year (therefore, having a higher and lower risk of falling, respectively). After signal pre-processing, ApEn and SampEn were calculated using 72 different combinations of input parameters. Standard methods for the statistical analysis of continuous data were used in order to (1) investigate the effects of changing input parameters on ApEn and SampEn on ApEn and SampEn values; (2) determine the ability of ApEn and SampEn to discriminate between groups, in particular between young adults, non-fallers and fallers; and, (3) identify specific combinations of input parameters revealing significant differences between groups.

The results of this study suggest that SampEn represents a better choice for the analysis of CoP time-series given its relative consistency and ability to discriminate between experimental groups. However, the selection of input parameter values proved to be critical in the identification of significant differences between older adults with and without falls in the last 12 months (i.e. fallers and non-fallers, respectively). In particular, significant differences were mostly observed in CoP time-series in the Anterior-Posterior (AP) direction of 60-s duration ($N = 1200$). Therefore, further studies using these entropy measures should favour longer CoP recordings (e.g. $\geq$ 60 seconds) over shorter CoP recordings (e.g. 30 seconds), as well as focus the analyses on AP time-series. Researchers and clinicians working on the

analysis of CoP time-series are recommended to use SampEn with input parameters $m = \{4, 5\}$ and $r = \{0.25, 0.3, 0.35\}$. The study has been published elsewhere [153].

Research question 3: Are there any associations between day-to-day variations in sleep quality, as measured via wearable sensors, and balance control?

Research question 4: What is the optimal method to capture variations in balance control due to day-to-day variations in sleep quality, linear or nonlinear measures?

Wearable devices offer new opportunities for in-home continuous sleep monitoring in the broader population. It is potentially relevant for fall risk assessment, given that chronic sleep disturbances and poor sleep quality are associated with further falls in older people. Hence, if short-lived sleep disturbances and poor sleep quality have a similar effect on balance control, continuous sleep monitoring would be relevant for fall prevention programmes in frail populations and sleep disturbance-inducing scenarios (e.g. hospital wards). Therefore, the potential association between day-to-day variations in sleep quality and balance control deficits warrants investigation.

Chapter 5 presented a study performed to investigate the potential use of wearable devices for capturing day-to-day variations in sleep quantity and quality, as well as the sensitivity of the balance control system to these variations. A sample of 20 young volunteers with no history of sleep disorders or balance impairments participated in the study. Sleep and balance were assessed over two consecutive days. Sleep quantity and quality variations were assessed using a sleep diary, actigraphy and Heart Rate Variability (HRV) measures. Sleep was monitored at home using an unobtrusive wearable device. Balance was assessed in a gait lab using foot CoP displacement during unperturbed standing. Subjects with a day-to-day deterioration in sleep quantity and quality (i.e., decreased duration and increased fragmentation, increased nocturnal activity and decreased HRV) exhibited significant changes in balance (i.e., larger CoP area, amplitude and standard deviation). Conversely, subjects with no significant alterations in sleep quantity and quality showed no significant changes in CoP displacements. Firstly, the results of this study suggest that wearable devices can be used for detecting day-to-day variations in sleep quantity and quality. In particular, the duration of rest periods and the presence of sleep disturbances can be estimated from acceleration and Electrocardiogram (ECG) signals. Moreover, the results suggest that day-to-day variations in

sleep quantity and quality affect balance control during unperturbed standing. This study has been published elsewhere [180].

In addition, chapter 6 presented a study performed to confirm and extend the findings of the studies mentioned earlier. Namely, this study investigated further the potential use of wearable devices for capturing day-to-day variations in sleep quantity and quality, as well as the sensitivity of the balance control system to these variations, in a sample of 31 young healthy volunteers, from which seven also participated in the study reported in chapter 5. As in the study above, sleep quantity and quality variations were assessed using sleep diary, actigraphy and HRV measures, the last two derived from an unobtrusive wearable device. Balance was assessed using net CoP displacement during unperturbed standing. In contrast with the previous study, the present study explored the sensitivity of SampEn to the differences in balance control produced by day-to-day variations in sleep quantity and quality. Subjects with a day-to-day deterioration in sleep quantity and quality (i.e., decreased duration and increased fragmentation, increased nocturnal activity and decreased HRV) exhibited significant changes in balance (i.e., slower and more regular CoP motion, in particular in the Medial-Lateral (ML) direction under the Eyes Closed (EC) testing condition). Conversely, subjects with no significant alterations in sleep quantity and quality showed no significant changes in CoP displacements. Firstly, the results of this study confirmed that wearable devices could be used for detecting day-to-day variations in sleep quantity and quality. Moreover, the results confirmed that day-to-day variations in sleep quantity and quality affect balance control during unperturbed standing. Both linear and nonlinear measures of CoP displacement captured these variations. Preliminary results of this study were presented elsewhere [202].

Overall, both studies show that wearable devices can be used to capture day-to-day variations in sleep quantity and quality, which in turn produce variations in balance. In particular, both studies show that self-reported sleep quality is associated with a sleep of short duration and higher fragmentation (i.e. interrupted sleep). However, the effects of poor sleep on balance control differ from one study to the other. In study 3 (chapter 5) the effects are observed on the AP direction, whereas in study 3 the effects are apparent on the ML direction. This heterogeneity has been previously in previous studies, which has precluded a firm conclusion about the optimal CoP measures for fall risk assessment in older adults [92]. Notwithstanding, both studies reveal a deterioration of balance control after poor sleep, with study 4 showing that both linear and nonlinear CoP measures are sensitive to this deterioration. This last observations provides a higher relevance to study 4.

7.4 Limitations and further work

This thesis and the studies herein produced relevant contributions to the body of knowledge related to the adoption of wearable sensors and nonlinear signal analysis methods for balance and fall risk assessment in older adults. However, due to time and resources constraints, this research presents some limitations, which provide the basis for a sketch of further work.

Firstly, the study presented in chapter 3 identified an optimal protocol for fall risk assessment in older adults using wearable inertial sensors, including optimal sensor placement, functional task and measured variables. Nevertheless, these results are based on data extracted from a limited number of studies. Hence, they are unable to provide a representative inference of all features used and all studies published, but not included in the review. This means that there might be some other sensor-based features that are discriminant between non-fallers and fallers but which were not included in this systematic review as they were not reported as required by the inclusion criteria. Further studies could validate the optimal protocol for fall risk assessment suggested in this thesis and explore further those features which have shown a consistent trend across different studies, but that were not found significant possibly due to the low number of studies pooled in the analysis and the heterogeneity between studies in terms of design (see Table 3.6).

Moreover, among the studies not included in the review, there are some whose focus is of interest to this research. Namely, some studies used wearable inertial sensors for collecting data related to gait quantity and quality during daily-life activities [56, 150, 151]. Moreover, some studies have reported significant associations between fall risk and nonlinear descriptors of gait dynamics (e.g. Multi-scale Entropy (MSE) and Recurrence Quantification Analysis (RQA) measures) [55, 149]. Although there is not enough evidence to support a firm conclusion, the results of these studies suggest that ambulatory gait monitoring combined with nonlinear descriptors of gait is a promising approach to fall risk assessment. Further research on this line is warranted.

The study presented in chapter 4 confirmed the ability of ApEn and SampEn to discriminate non-fallers from fallers and identified the optimal usage of these nonlinear measures. However, it must be acknowledged that there are more recent developments in the field of nonlinear analysis that could potentially improve the sensitivity when looking for differences between groups. In particular, the development of multiscale entropy and multivariate MSE have offered new perspectives for the analysis of biological time-series [163–166]. A few studies have already applied

these approaches to the analysis of CoP time-series [99, 105, 107]. Briefly, MSE relies on the computation of sample entropy values at different time-scales and produces a two-dimensional plot (time-scale versus sample entropy) depicting a profile line for each experimental group/condition. An overall entropy 'score' can be computed by adding the entropy values at specific time-scales [105]. While MSE represents an interesting tool to explore the level of regularity contained at different time-scales, it cannot avoid the issue of the adequate selection of input parameters. Since MSE and its variations are based on SampEn, researchers that opt for MSE face essentially the same problem faced when 'single-scale' entropy measures are used; i.e. the adequate selection of input parameters. Further studies could investigate the ability of MSE to discriminate non-fallers from fallers, leveraging on the findings presented in this thesis regarding optimal parameter selection or at least the adoption of a systematic approach to the identification of optimal parameters.

The studies presented in chapters 5 and 6 confirmed the ability of wearable devices for capturing day-to-day variations in sleep quantity and quality. However, the methods related to sleep assessment used in this research require further development to produce sleep parameters more relevant for the user and clinician (e.g. time in light and deep sleep). This was not possible due to the lack of annotated data (e.g. knowing the actual sleep stage for each epoch). Therefore, further studies should consider collecting chest actigraphy, ECG and polysomnography data concurrently, in order to develop novel sleep staging algorithms based on activity and HRV measures [36]. Moreover, future studies should also investigate whether the actual wearing of body-attached sensors alters sleep quantity and quality in older adults. This and other aspects (e.g. perceived usefulness and social influence) are considered as potential determinants of wearable technology acceptance among older adults and thus warrant further investigation [204].

Finally, the studies in chapters 5 and 6 also confirmed the sensitivity of the balance control system to day-to-day variations in sleep quantity and quality. However, the neurophysiological mechanisms behind the observed alterations in postural control cannot be elucidated from the data collected. Also, these studies enrolled young adults, yet the primary interest is on fall risk assessment in older adults. Therefore, further studies should enrol older adults and evaluate balance under more testing conditions in order to detect and identify underlying mechanisms.

7.5 Final remarks

Wearable sensors and nonlinear signal analysis methods are empowering innovative ways of assessing balance and fall risk in older adults. However, their adoption in research and clinical practice poses some challenges. This thesis and the studies herein addressed some of those challenges and provided some insights concerning their optimal use.

Indeed, wearable inertial sensors offer the means for developing instrumented versions of clinical balance assessment tools, producing objective and accurate quantitative descriptors on the timing and execution of functional tasks. However, this research proved that selecting an adequate combination of sensor placement, movement task and measured variable is crucial for discriminating subjects at a higher risk of falling. An optimal protocol for assessing fall risk based on wearable inertial sensors was identified.

Additionally, wearable devices offer the means for continuously monitoring physiological and behavioural variables, which can be used to infer outcomes linked to impaired balance and increased risk of falling. This research proved that wearable devices could be used to capture day-to-day variations in sleep quantity and quality, which in turn produce variations in balance. This situation can potentially expand the prevailing paradigm in fall prevention, from the current one focusing on the occasional assessment of risk factors and changes in the balance control system to a new paradigm including also the continuous monitoring and detection of short-lived factors that might result in an imminent fall.

Finally, this research proved that quantitative descriptors of nonlinear dynamics are more sensitive than linear measures to differences in balance control due to ageing and risk of falling (e.g. non-fallers and fallers). However, it was also shown that the adequate selection of the input parameters required for their computation is of paramount importance to achieve positive results. This thesis provided some recommendations for the parameter selection.

Collectively, the findings of this research confirm that wearable sensors and nonlinear signal analysis methods can improve and extend current tools and practices in balance and fall risk assessment.

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Appendix A

Source codes listings

Listing A.1: R script for the statistical analysis of the inertial sensor-based features

```
#Preparing the environment
require(dplyr)
require(vcd)


# Loading and preparing data
features = read.csv("features.csv");
features$Significance = as.factor(features$Significance);
sfeatures = filter(features, features$Significance == "Significant");

# Getting familiar with the data
summary(features);
summary(sfeatures);


# Count and proportion of features per family/task/sensor placement/
    study
summary(features$Category)
round(prop.table(summary(features$Category))*100,1)

summary(features$Task)
round(prop.table(summary(features$Task))*100,1)

summary(features$Sensor.placement)
round(prop.table(summary(features$Sensor.placement))*100,1)

summary(features$Study)
round(prop.table(summary(features$Study))*100,1)

summary(sfeatures$Category)
```

```
round(prop.table(summary(sfeatures$Category))*100,1)

summary(sfeatures$Task)
round(prop.table(summary(sfeatures$Task))*100,1)

summary(sfeatures$Sensor.placement)
round(prop.table(summary(sfeatures$Sensor.placement))*100,1)

summary(sfeatures$Study)
round(prop.table(summary(sfeatures$Study))*100,1)

# Tests and measures of association for 2-way contingency tables
task.signif = xtabs(~Task + Significance, data = features);
addmargins(task.signif);
summary(assocstats(task.signif));

placement.signif = xtabs(~Sensor.placement + Significance, data =
    features);
addmargins(placement.signif);
summary(assocstats(placement.signif));

category.signif = xtabs(~Category + Significance, data = features);
addmargins(category.signif);
summary(assocstats(category.signif));

study.signif = xtabs(~Study + Significance, data = features);
addmargins(study.signif);
summary(assocstats(study.signif));


#Second step
sfeatures = droplevels(sfeatures);

task.placement = xtabs(~Task + Sensor.placement, data = sfeatures);
addmargins(task.placement);
summary(assocstats(task.placement));
round((task.placement-independence_table(task.placement))/sqrt(
    independence_table(task.placement)), 1);
assoc(task.placement, shade = TRUE);

task.category = xtabs(~Task + Category, data = sfeatures);
addmargins(task.category);
summary(task.category);
round((task.category-independence_table(task.category))/sqrt(
    independence_table(task.category)), 1);
assoc(task.category, shade = TRUE);
```

```
73
74 category.placement = xtabs(~Category + Sensor.placement, data =
       sfeatures);
75 addmargins(category.placement);
76 summary(assocstats(category.placement));
77 round((category.placement-independence_table(category.placement))/sqrt(
       independence_table(category.placement)), 1);
78 assoc(category.placement, shade = TRUE);
79
80
81 three.way.table = xtabs(~Category + Task + Sensor.placement, data =
       sfeatures)
82 structable(three.way.table)
83 summary(three.way.table)
84 round((three.way.table-independence_table(three.way.table))/sqrt(
       independence_table(three.way.table)),1)
85 assoc(three.way.table, shade = TRUE)
```

Listing A.2: R script for the meta-analysis of the inertial sensor-based features

```
## Loading required packages
require(XLConnect)
require(meta)

# Loading features data from file
wb = loadWorkbook("features.xlsx")
N = length(getSheets(wb));

# Running analysis
pooled = data.frame(Outcome = character(), I2 = numeric(), Q = numeric(),
                    p = numeric(), Model = character(), Subjects = numeric(),
                    MD = numeric(), CI_lower = numeric(), CI_upper = numeric(),
                    pvalue = numeric())
mdl_type = matrix(nrow = N, ncol = 1)

for(i in 1:N) {

    outcome = readWorksheet(wb, sheet = i)
    mdl = metacont(F.N, F.Mean, F.SD, NF.N, NF.Mean, NF.SD, data = outcome,
                   studlab = Study, label.e = "Fallers", label.c = "Non-Fallers")
    I2 = round(mdl$I2*100,1)
    Q = round(mdl$Q, 2)
    p = round(pchisq(mdl$Q, mdl$df.Q, lower.tail = FALSE), 4)

    pooled[i, 2] = I2
    pooled[i, 3] = Q
    pooled[i, 4] = p
    pooled[i, 6] = sum(mdl$n.e)+sum(mdl$n.c)

    if(I2 < 60 || p > 0.1) {
        mdl_type[i] = "Fixed"
        pooled[i, 7] = round(mdl$TE.fixed, 4)
        pooled[i, 8] = round(mdl$lower.fixed, 4)
        pooled[i, 9] = round(mdl$upper.fixed, 4)
        pooled[i, 10] = round(mdl$pval.fixed, 4)
    }
    else {
        mdl_type[i] = "Random"
        pooled[i, 7] = round(mdl$TE.random, 4)
        pooled[i, 8] = round(mdl$lower.random, 4)
```

```
41            pooled[i, 9] = round(mdl$upper.random, 4)
42            pooled[i, 10] = round(mdl$pval.random, 4)
43        }
44
45    }
46
47    pooled$Outcome = getSheets(wb)
48    pooled$Model = mdl_type
49
50    # Displaying and printing pooled features data.frame
51    View(pooled)
52    print(pooled)
53
54    # Writing pooled features to CSV file
55    write.csv(pooled, file = "pooled.csv")
56
57    # Cleaning environment
58    rm(list=ls())
```

Listing A.3: MATLAB function for CoP time-series preprocessing

```
function [CPap, CPml] = preprocessingCoP(CPap, CPml, fs, fc)
% preprocessingCoP
%   Applies preprocessing operations to centre of pressure (CoP)
%   time-series: filtering and detrending (mean value substraction)
%
%   INPUTS: CPap= input 1dim array containing the raw CoP time-series
    for
%   the anterior-posterior direction; CPml= input 1dim array containing
    the
%   raw CoP time-series for the medial-lateral direction; fs= original
%   sampling frequency of the CoP time-series; fc= cut-off frequency of
    the
%   filter
%
%   OUTPUTS: CPap= output 1dim array containing the processed CoP
%   time-series for the anterior-posterior direction; CPml= output 1dim
%   array containing the processed CoP time-series for the medial-
    lateral
%   direction

%% Filtering: 4th-order Butterworth low-pass filter
[z,p,k] = butter(4, (2*fc)/fs, 'low');
[sos, g] = zp2sos(z, p, k);

% Zero phase filtering
CPap = filtfilt(sos, g, CPap);
CPml = filtfilt(sos, g, CPml);

%% Detrending: Mean value substraction
CPap = CPap - mean(CPap);
CPml = CPml - mean(CPml);

end
```

Listing A.4: MATLAB functions for global CoP measures calculation.

```
function globalCoPtbl = globalCoP(CPap, CPml, fs)
%% globalCoP
%   Calculates features for the global analysis of the Center of
    Pressure
%   (CoP) as described in:
%
%   Duarte, M., & Freitas, S. M. (2010). Revision of posturography
    based on
%   force plate for balance evaluation. Brazilian Journal of Physical
%   Therapy, 14(3), 183 192.
%
%   INPUTS: CPap= input 1dim array containing the CoP time-series for
    the
%   anterior-posterior direction; CPml= input 1dim array containing the
     CoP
%   time-series for the medial-lateral direction; fs= sampling
    frequency of
%   the CoP time-series
%
%   OUTPUTS: globalCoPtbl= 1x9 table containing computed global CoP
%   measures


%% Computing features calling to specific functions (below)
dot = DOT(CPap, CPml);
[SDap, SDml] = SD(CPap, CPml);
[AdCPap, AdCPml] = AdCP(CPap, CPml);
[TMV, MVap, MVml] = MV(CPap, CPml, fs);
area = Area(CPap, CPml);

%% Creating output table
FeatureNames = {'DOT', 'SDap', 'SDml', 'AdCPap', 'AdCPml',...
    'TMV', 'MVap', 'MVml', 'Area'};
globalCoPtbl = table(dot, SDap, SDml, AdCPap, AdCPml, TMV, MVap, MVml,
    area,...
    'VariableNames', FeatureNames);

end


%% DOT, Total length
function DOT = DOT(CPap, CPml)

DOT = sum(sqrt(diff(CPap).^2 + diff(CPml).^2));

```

```
40 end
41
42
43 %% Standard deviation
44 function [SDap, SDml] = SD(CPap, CPml)
45
46 SDap = std(CPap);
47 SDml = std(CPml);
48
49 end
50
51
52 %% Amplitud of displacement
53 function [AdCPap, AdCPml] = AdCP(CPap, CPml)
54
55 AdCPap = abs(max(CPap)-min(CPap));
56 AdCPml = abs(max(CPml)-min(CPml));
57
58 end
59
60
61 %% Mean velocity: AP (MVap), ML (MVml) and total (TMV)
62 function [TMV, MVap, MVml] = MV(CPap, CPml, fs)
63 %t:Length of CoP signal (seconds)
64 t = length(CPap)/fs;
65
66 %Calculation of the total CoP velocity
67 TMV = sum(sqrt(diff(CPap).^2 + diff(CPml).^2)) / t;
68
69 %Calculation of CoP velocity in the ML direction
70 MVml = sum(sqrt(diff(CPml).^2)) / t;
71
72 %Calculation of CoP velocity in the AP direction
73 MVap = sum(sqrt(diff(CPap).^2)) / t;
74
75 end
76
77
78 %% Area
79 function Area = Area(CPap, CPml)
80
81 [vec,val] = eig(cov(CPap,CPml));
82 Area = pi*prod(2.4478*sqrt(svd(val)));
83
84 end
```

Listing A.5: MATLAB function for approximate entropy (ApEn) computation

```
function ApEn = ApEn(u, m, r)
%% ApEn
% Estimates approximate entropy (ApEn) from a time-series as described in:
%
% Pincus, S. M., Gladstone, I. M., & Ehrenkranz, R. A. (1991). A regularity
% statistic for medical data analysis. Journal of Clinical Monitoring and
% Computing, 7(4), 335 345.
%
% INPUTS: u= input time series; m= subseries length; r= similarity
% tolerance
%
% OUTPUT: ApEn= ApEn value

N = length(u);
phi = zeros(1,2);

for iter = 1:2
    dim = m+iter-1;
    C = zeros(1, N-dim+1);
    X = zeros(dim, N-dim+1);

    % Form subseries X(1), X(2), ..., X(N):
    if dim == 1
        X = u;
    else
        for i = 1:dim
            X(i,:) = u(i:N-dim+i);
        end
    end

    % For each X(i), find C:
    for i = 1:N-dim+1
        % Distance between subseries
        if dim == 1
            d = abs(X - repmat(X(:,i), 1, N-dim+1));
        else
            d = max(abs(X - repmat(X(:,i), 1, N-dim+1)));
        end

        % Check if distances are less than the tolerance level
        bool = any(d < r*std(u), 1);

```

```
43          % Calculate C
44          C(i) = sum(bool)/(N-dim+1);
45      end
46
47      % Calculate phi
48      phi(iter) = mean(log(C));
49  end
50
51  %Estimate ApEn
52  ApEn = phi(1) - phi(2);
53
54  end
```

Listing A.6: MATLAB function for sample entropy(SampEn) computation

```
function SampEn = SampEn(u, m, r)
%% SampEn
% Estimates sample entropy (SampEn) from a time-series as described in:
%
% Richman, J. S., & Moorman, J. R. (2000). Physiological time-series
% analysis using approximate entropy and sample entropy. American
    Journal
% of Physiology-Heart and Circulatory Physiology, 278(6), H2039H2049.
%
% INPUTS: u= input time series; m= subseries length; r= similarity
% tolerance
%
% OUTPUT: SampEn= SampEn value

N = length(u);
B_A = zeros(1,2);

for iter = 1:2
    dim = m + iter -1;
    X = zeros(dim, N-dim+1);
    N_matches = zeros(1, N-dim);

    % Form subseries X(1), X(2), ..., X(N):
    if dim == 1
        X = u;
    else
        for i = 1:dim
            X(i,:) = u(i:N-dim+i);
        end
    end

    % Find Ni
    for i = 1:N-dim
        % Distance between subseries
        if dim == 1
            d = abs(X - repmat(X(:,i), 1, N-dim+1));
        else
            d = max(abs(X - repmat(X(:,i), 1, N-dim+1)));
        end
        % Check if distances are less than the tolerance level
        bool = (d <= r*std(u));
        % Find number of d < r * SD_u minus 1 to discard self-match
        N_matches(i) = (sum(bool)-1);
    end

```

```
45      % Calculate Bi (when iter=1) and Ai (when iter=2)
46      Bi_Ai = N_matches/(N-dim-1);
47      % Calculate B (when iter=1) and A (when iter=2)
48      B_A(iter) = mean(Bi_Ai);
49  end
50
51  %Estimate SampEn
52  SampEn = -log(B_A(2)/B_A(1));
53
54  end
```

Listing A.7: MATLAB function for Zero Crossing Mode implementation

```
function ZCM_data = ZCM(VMU_data)
% ZCM
%   Calculates activity counts for 1-minute epochs using the Zero-Crossing
%   Mode (ZCM) as described in:
%
%   Jean-Louis, G., Kripke, D. F., Mason, W. J., Elliott, J. A., &
%   Youngstedt, S. D. (2001). Sleep estimation from wrist movement
%   quantified by different actigraphic modalities. Journal of Neuroscience
%   Methods, 105(2), 185 191.
%
%   INPUT: VMU_data= input acceleration data, fs=1Hz,
%
%   OUTPUT: ZCM_data= activity counts for 1-min epochs

Nepochs = floor(length(VMU_data)/60); % Number of epochs to be generated
T = 0.1;

for i = 0:Nepochs-1
    counter = 0;
    index1 = i*60 + 1;
    index2 = i*60 + 60;

    for j = index1:index2 - 1
        if((VMU_data(j)<T & VMU_data(j+1)>T) | (VMU_data(j)>T & VMU_data(j+1)<T))
            counter = counter+1;
        end
    end

    ZCM_data(i+1) = counter;

end

end
```

Listing A.8: MATLAB function for Activity measures calculation

```
function ACTmeasures = ACT(ZCM_data, Posture)
% ACT
%    Calculates activity measures from activity counts (1-min epochs) and
%    posture data
%
%    INPUTS: ZCM_data= 1-dim array of length N containing activity counts
%    for N 1-min epochs; Posture= posture data as reported by the Zephyr BH3
%
%    OUTPUT: ACTtbl= 1x6 table containing activity measures

% Preparing Posture data
Posture = downsample(Posture, 60); % Downsampling to 1 sample/minute
Posture = Posture(1:length(ZCM_data));

% Finding Bed Time (BT) and and Out-of-Bed Time (OBT)
[BT OBT] = findBedTime(Posture, 50, 15);

% Segment signal: Time in Bed
ZCM_data_TIB = ZCM_data(BT:OBT);

% Computes activity measures by calling specific functions (below)
ACTmeasures(1) = mean(ZCM_data_TIB);      %ACT_mean
ACTmeasures(2) = std(ZCM_data_TIB);       %ACT_sd
ACTmeasures(3) = AI(ZCM_data_TIB);        %AI
[ACTmeasures(4) ACTmeasures(5) ACTmeasures(6)] = FI(ZCM_data_TIB);

ACTmeasures = array2table(ACTmeasures,'VariableNames',...
    {'ACT_mean','ACT_sd','ACT_AI','ACT_FI','ACT_I_max','ACT_I_mean'});

end


function [BT OBT] = findBedTime(Posture_data, Angle, Window)
%% findBedTime

% If subject is facing up/down then Pbin = 0; (upright) else Pbin = 1
Posture_bin = abs(Posture_data) < Angle;

% Finding Bed Time
for i = 1:length(Posture_bin)
    if(Posture_bin(i : i + Window) == 0)
        BT = i;
```

```
43          break;
44      end
45  end
46
47  % Finding Out-of_Bed Time (OBT)
48  for i=length(Posture_bin):-1:1+Window
49      if(Posture_bin(i-Window:i) == 0)
50          OBT = i;
51          break;
52      end
53  end
54
55  end
56
57  function ai = AI(data)
58  %% Activity Index
59  ai = (sum(data>0)/length(data))*100;
60  end
61
62  function [fi I_max I_mean] = FI(data)
63  %% Fragmentation Index
64
65  RestBouts = zeros(720,1);
66  counter = 1;
67  for i=2:length(data)
68      if(data(i)==0)
69          if(data(i-1)~=0)
70              counter = counter + 1;
71              RestBouts(counter) = RestBouts(counter) + 1;
72          else
73              RestBouts(counter) = RestBouts(counter) + 1;
74          end
75      end
76  end
77
78  RestBouts = RestBouts(RestBouts~=0);
79
80  fi = (sum(RestBouts<=5) / length(RestBouts))*100;
81  I_max = max(RestBouts);
82  I_mean = mean(RestBouts);
83
84  end
```

Appendix B

Supplementary materials for study 1

Document S1. Checklist for Study Quality Appraisal

Study identification (include author(s), title, year of publication, journal title, pages)

	Yes=1 No/Unclear=0
Reporting	
Aim/Objective	
1) Is the hypothesis/aim/objective of the study clearly described?	
Materials & Methods	
2) Are study participants' inclusion/exclusion criteria clearly stated?	
3) Is the experimental protocol clearly described? The experimental protocol must include at least a description of the way in which subjects were labelled as fallers and non-fallers, the task(s) they were requiered to perform and the number and placement of sensors used during the experiments.	
4) Are sensors' technical specifications provided? Alternatively, product name, model and manufacturer must be provided.	
5) Are the main methods for signal preprocessing clearly described or properly referenced?	
6) Are the main methods for feature extraction clearly described or properly referenced?	
7) Are the statistical analysis clearly described and appropiate?	
Results	
8) Is the age of participants included in both groups clearly stated?	
9) Are the distributions of principal confounders (other than age; e.g. BMI, medication, comorbidities, etc) in each group of subjects to be compared clearly described?	
10) Are summary statistics (mean and standard deviation) provided for all features described in the methods?	
11) Have actual probability values been reported (e.g. 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	
External validity	
12) Were study participants representative of the population under investigation?	
13) Was the activity assessed representative of clinical fall risk assessment protocols or the daily life activities?	
Internal validity - Bias & Confounding	
14) Were the subjects in different groups (non-fallers and fallers) recruited from source populations that are comparable in all aspects other than fall status and over the same period of time?	
15) Was the study designed and conducted to minimise the risk of bias and confounding and to establish a relationship between measures and fall status?	
SUM	

Appendix C

Supplementary materials for study 2

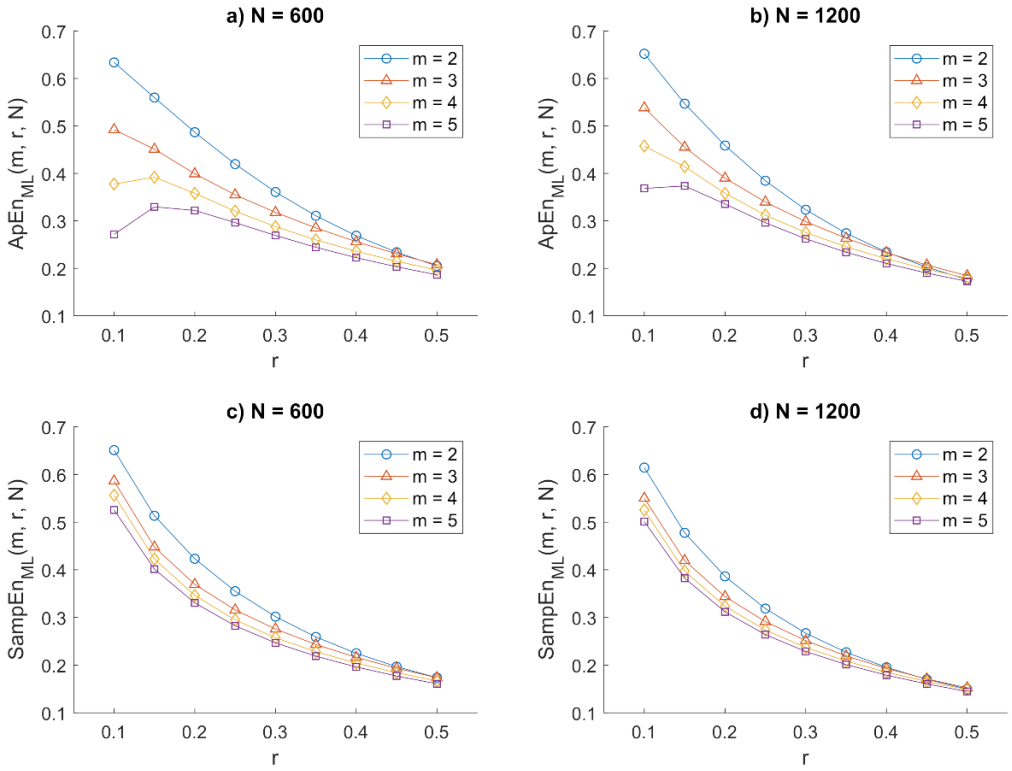

Fig. S1 Approximate entropy (ApEn) and sample entropy (SampEn) as a function of m, r and N for the medial-lateral (ML) component of the centre of pressure displacement during quiet standing.

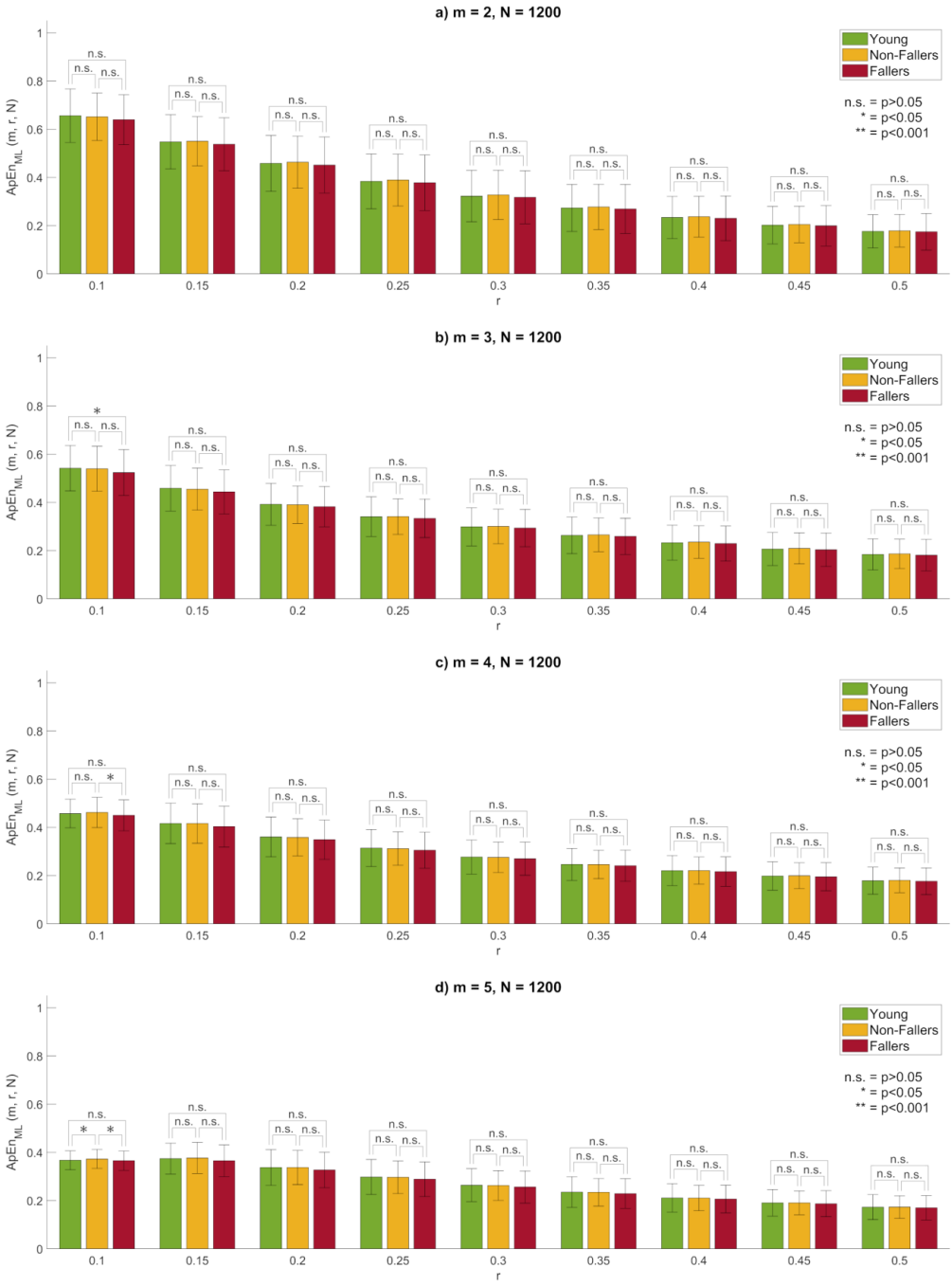

Fig. S2 Approximate entropy (ApEn) mean value (bars) and standard deviation (error lines) by group as a function of r for $m = \{2, 3, 4, 5\}$ (from top to bottom) and $N = 1200$ (i.e. 60 seconds) for the medial-lateral (ML) component of the centre of pressure displacement during quiet standing.

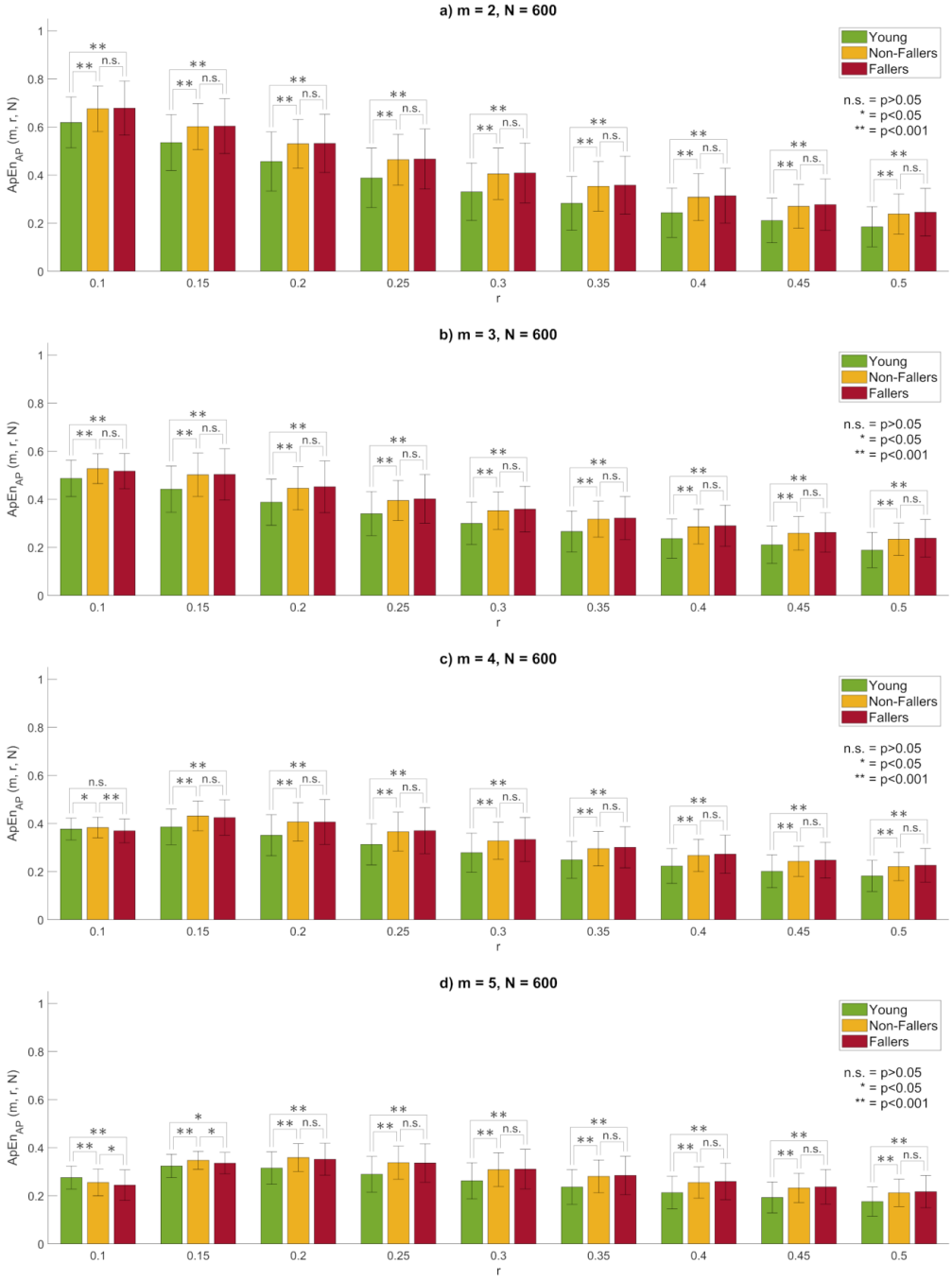

Fig. S3 Approximate entropy (ApEn) mean value (bars) and standard deviation (error lines) by group as a function of r for m = {2, 3, 4, 5} (from top to bottom) and N = 600 (i.e. 30 seconds) for the anterior-posterior (AP) component of the centre of pressure displacement during quiet standing.

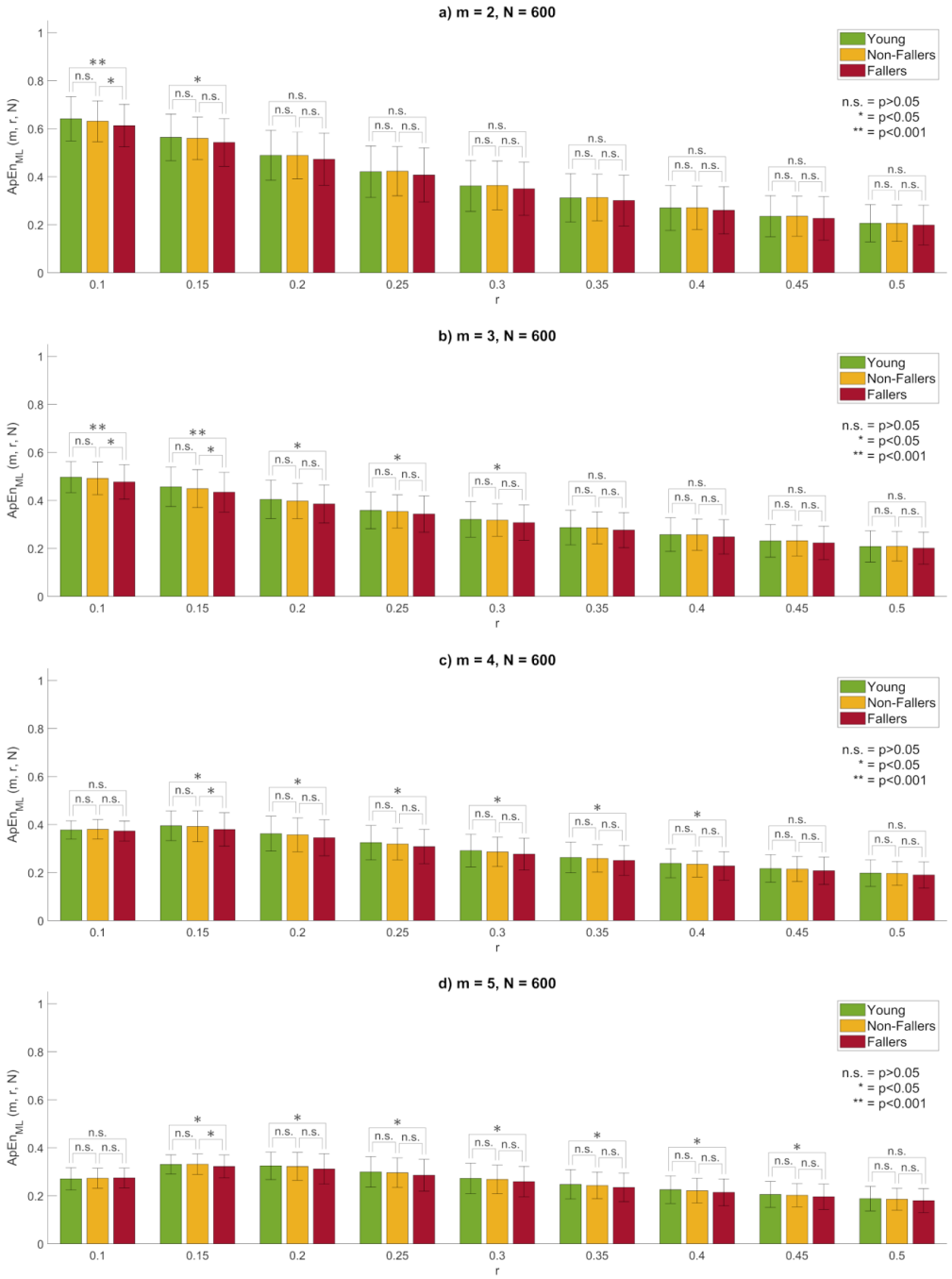

Fig. S4 Approximate entropy (ApEn) mean value (bars) and standard deviation (error lines) by group as a function of r for m = {2, 3, 4, 5} (from top to bottom) and N = 600 (i.e. 30 seconds) for the medial-lateral (ML) component of the centre of pressure displacement during quiet standing.

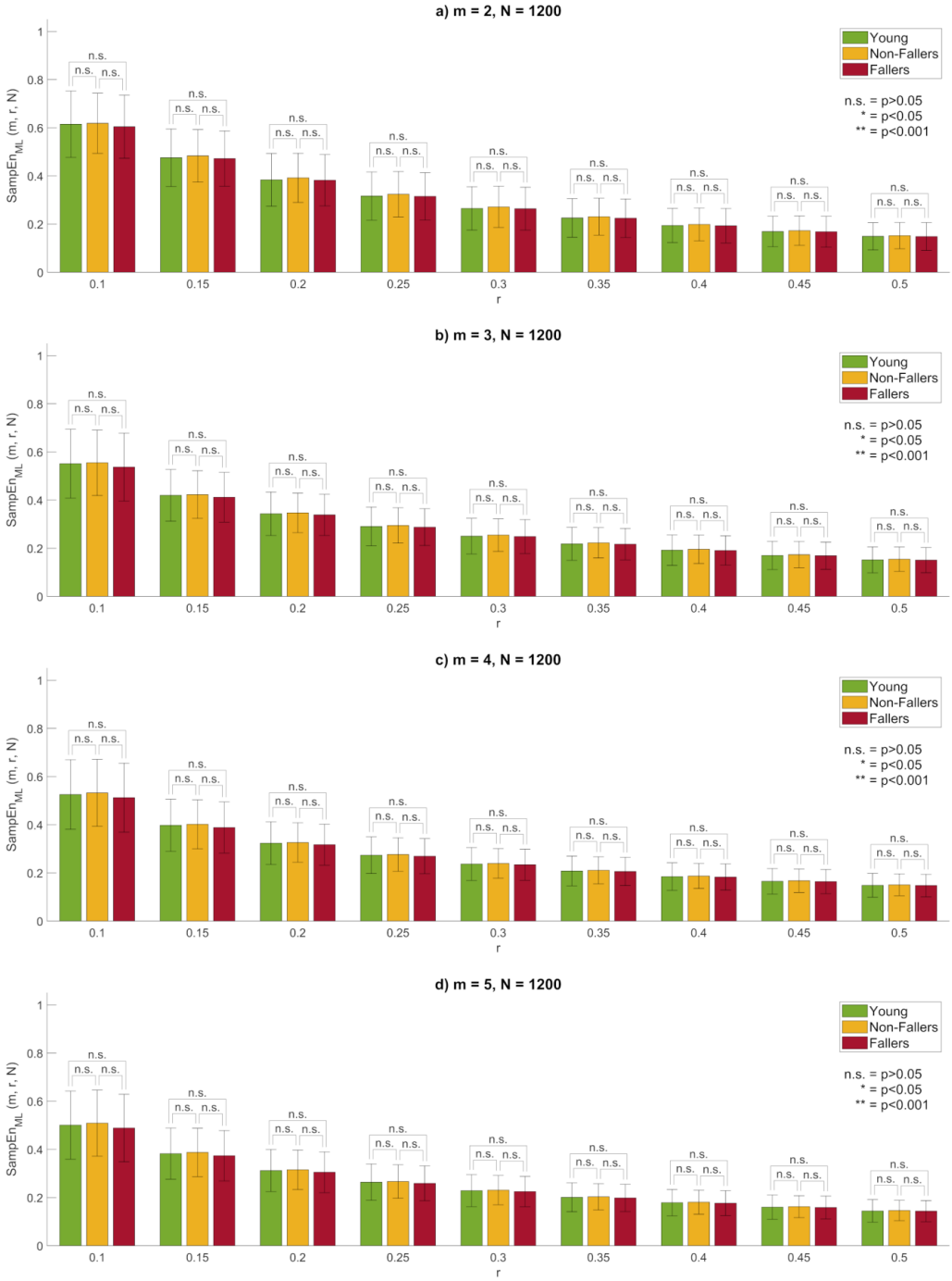

Fig. S5 Sample entropy (SampEn) mean value (bars) and standard deviation (error lines) by group as a function of r for $m = \{2, 3, 4, 5\}$ (from top to bottom) and $N = 1200$ (i.e. 60 seconds) for the medial-lateral (ML) component of the centre of pressure displacement during quiet standing.

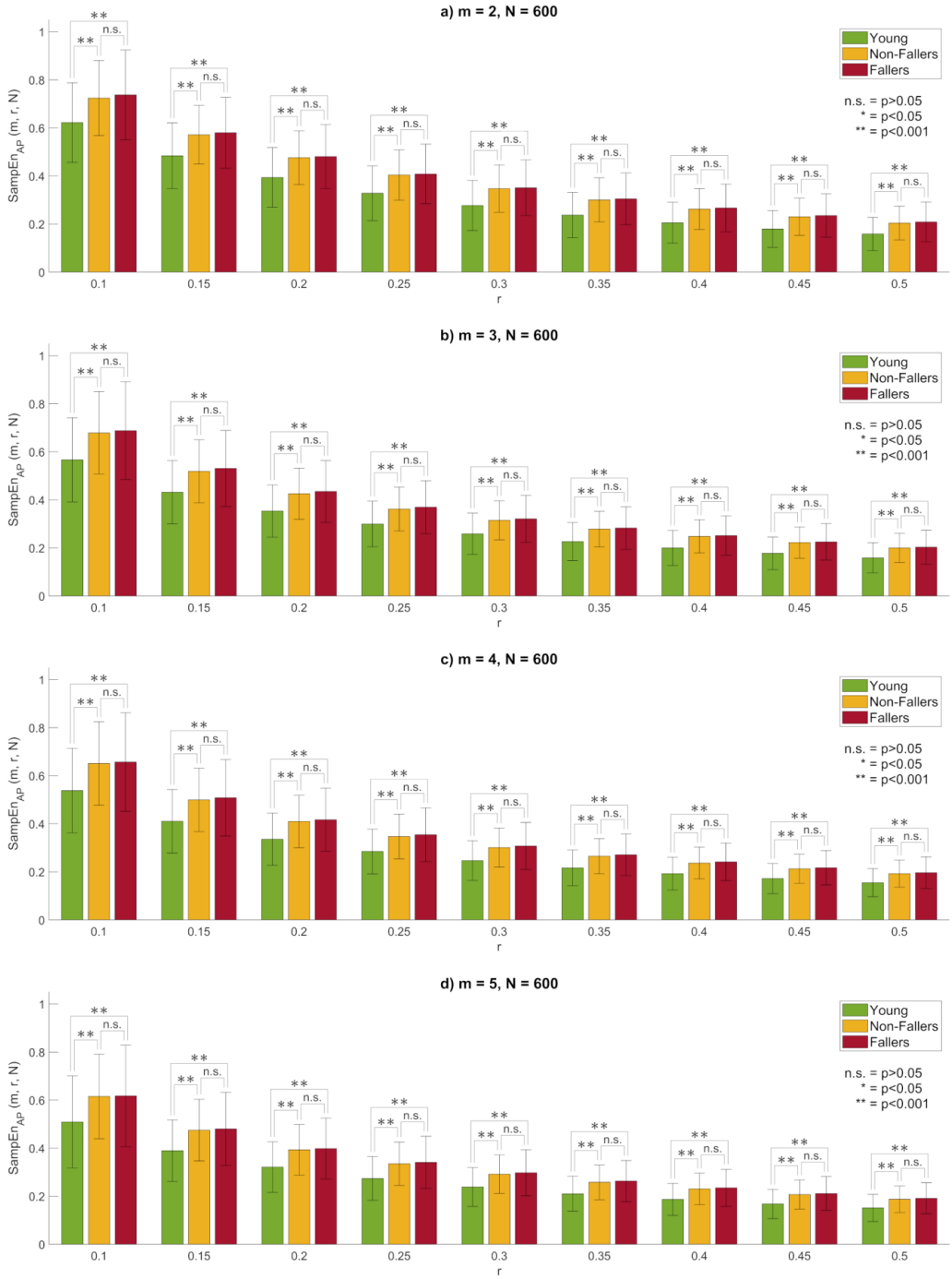

Fig. S6 Sample entropy (SampEn) mean value (bars) and standard deviation (error lines) by group as a function of r for m = {2, 3, 4, 5} (from top to bottom) and N = 600 (i.e. 30 seconds) for the anterior-posterior (AP) component of the centre of pressure displacement during quiet standing.

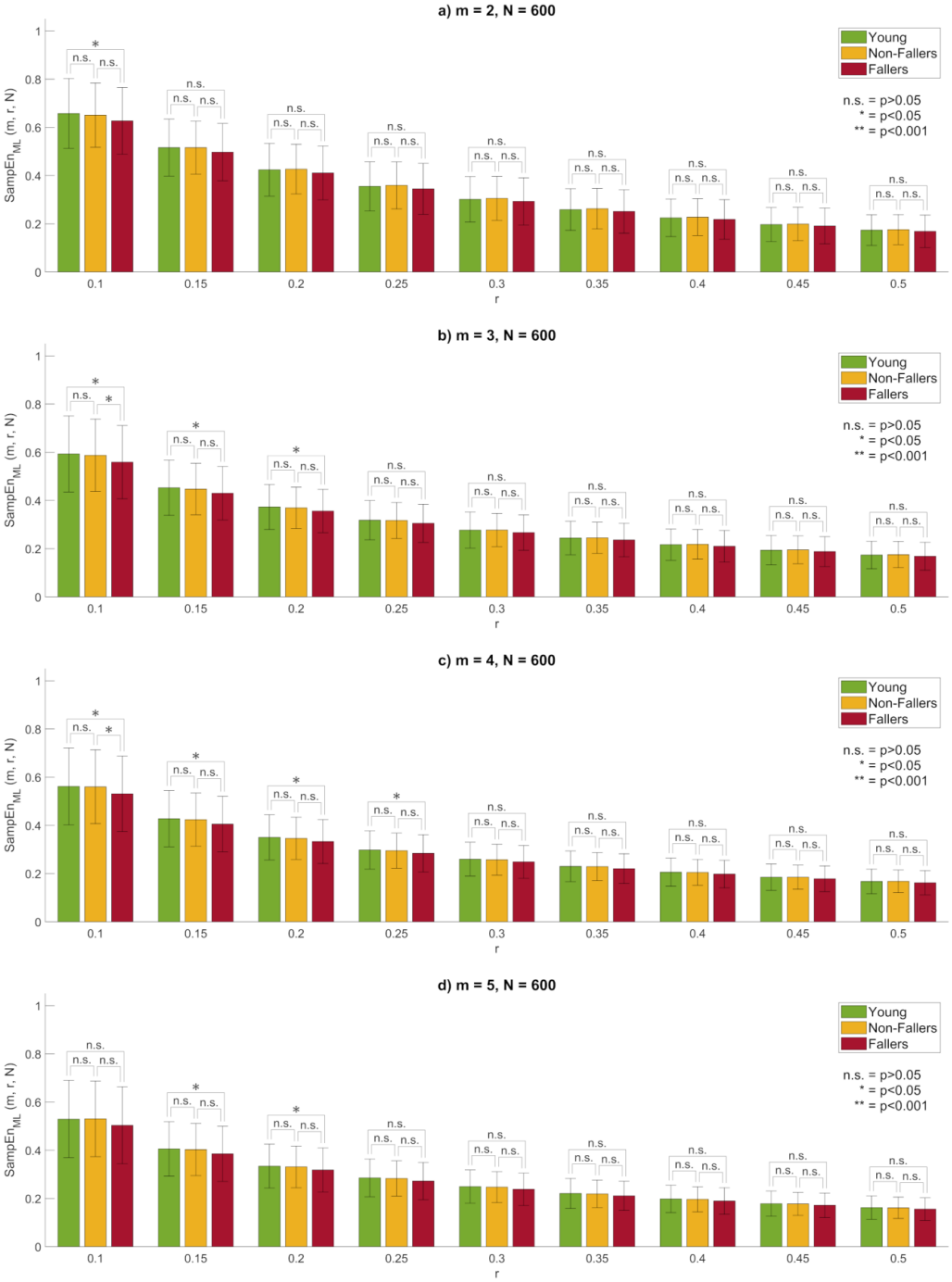

Fig. S7 Sample entropy (SampEn) mean value (bars) and standard deviation (error lines) by group as a function of r for $m = \{2, 3, 4, 5\}$ (from top to bottom) and $N = 600$ (i.e. 30 seconds) for the medial-lateral (ML) component of the centre of pressure displacement during quiet standing.

Table S2 Approximate entropy in the medial-lateral direction as a function of *r* and *m* for a data length of *N*=1200 (i.e. 60-seconds).

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	2.21	0.110	0.656	0.111	0.651	0.098	0.639	0.104	-0.005	0.660	-0.017	0.096	-0.012	0.324
0.15	1.05	0.349	0.548	0.113	0.550	0.102	0.538	0.110	0.002	0.898	-0.010	0.442	-0.012	0.317
0.2	0.97	0.380	0.458	0.116	0.463	0.108	0.451	0.116	0.005	0.638	-0.007	0.713	-0.012	0.382
0.25	0.97	0.378	0.384	0.114	0.389	0.108	0.378	0.116	0.006	0.577	-0.006	0.776	-0.011	0.405
0.3	0.87	0.419	0.323	0.107	0.328	0.102	0.318	0.110	0.005	0.611	-0.005	0.798	-0.010	0.447
0.35	0.73	0.481	0.273	0.098	0.278	0.094	0.269	0.102	0.004	0.657	-0.004	0.832	-0.008	0.510
0.4	0.61	0.541	0.234	0.088	0.237	0.085	0.230	0.093	0.003	0.709	-0.004	0.850	-0.007	0.564
0.45	0.49	0.612	0.202	0.078	0.205	0.076	0.199	0.084	0.003	0.742	-0.003	0.895	-0.005	0.643
0.5	0.40	0.673	0.176	0.069	0.179	0.067	0.174	0.076	0.002	0.772	-0.002	0.928	-0.004	0.711
m = 3														
0.1	3.14	**0.043**	0.542	0.094	0.540	0.093	0.524	0.095	-0.002	0.889	-0.018	**0.033**	-0.016	0.090
0.15	2.30	0.100	0.459	0.095	0.455	0.087	0.444	0.092	-0.003	0.738	-0.015	0.082	-0.011	0.256
0.2	1.20	0.303	0.392	0.087	0.390	0.078	0.382	0.084	-0.002	0.916	-0.010	0.269	-0.008	0.437
0.25	0.74	0.477	0.341	0.082	0.341	0.074	0.334	0.080	0	0.999	-0.007	0.476	-0.007	0.488
0.3	0.62	0.536	0.299	0.079	0.300	0.072	0.294	0.077	0.002	0.913	-0.005	0.642	-0.007	0.504
0.35	0.65	0.520	0.263	0.076	0.266	0.070	0.259	0.075	0.002	0.798	-0.004	0.735	-0.007	0.501
0.4	0.68	0.509	0.233	0.073	0.236	0.068	0.229	0.073	0.003	0.735	-0.004	0.784	-0.006	0.509
0.45	0.70	0.498	0.207	0.069	0.209	0.065	0.204	0.069	0.003	0.694	-0.003	0.813	-0.006	0.513
0.5	0.66	0.515	0.184	0.064	0.187	0.061	0.181	0.065	0.003	0.693	-0.003	0.835	-0.005	0.537
m = 4														
0.1	3.26	**0.039**	0.458	0.060	0.462	0.063	0.450	0.064	0.004	0.336	-0.008	0.211	-0.012	**0.033**
0.15	2.34	0.096	0.417	0.084	0.416	0.082	0.403	0.085	0	0.998	-0.013	0.089	-0.013	0.118
0.2	1.82	0.163	0.361	0.083	0.359	0.077	0.349	0.082	-0.002	0.882	-0.012	0.137	-0.010	0.280
0.25	1.31	0.269	0.314	0.077	0.312	0.069	0.305	0.075	-0.002	0.831	-0.009	0.241	-0.007	0.468
0.3	0.87	0.419	0.277	0.071	0.276	0.063	0.270	0.069	-0.001	0.932	-0.007	0.385	-0.006	0.554
0.35	0.61	0.543	0.246	0.066	0.246	0.059	0.241	0.064	0	0.995	-0.005	0.521	-0.005	0.590
0.4	0.47	0.627	0.221	0.063	0.221	0.056	0.217	0.061	0.001	0.983	-0.004	0.658	-0.004	0.612
0.45	0.44	0.645	0.198	0.059	0.200	0.054	0.195	0.058	0.001	0.920	-0.003	0.751	-0.004	0.618
0.5	0.46	0.633	0.179	0.056	0.181	0.051	0.177	0.055	0.001	0.861	-0.003	0.799	-0.004	0.615
m = 5														
0.1	4.98	**0.007**	0.367	0.039	0.373	0.039	0.365	0.040	0.006	**0.013**	-0.002	0.814	-0.007	**0.046**
0.15	2.63	0.072	0.374	0.064	0.377	0.064	0.365	0.066	0.003	0.654	-0.009	0.164	-0.012	0.057
0.2	1.88	0.153	0.337	0.074	0.337	0.071	0.327	0.074	0	1	-0.010	0.146	-0.010	0.173
0.25	1.47	0.230	0.298	0.073	0.297	0.068	0.289	0.072	-0.001	0.949	-0.009	0.202	-0.008	0.320
0.3	1.21	0.300	0.264	0.068	0.263	0.062	0.256	0.067	-0.001	0.902	-0.008	0.266	-0.006	0.446
0.35	0.93	0.396	0.235	0.064	0.234	0.057	0.229	0.061	-0.001	0.926	-0.006	0.362	-0.005	0.535
0.4	0.60	0.547	0.211	0.059	0.211	0.053	0.207	0.057	-0.001	0.975	-0.005	0.516	-0.004	0.631
0.45	0.44	0.645	0.191	0.055	0.191	0.049	0.187	0.054	0	0.999	-0.004	0.630	-0.004	0.676
0.5	0.33	0.717	0.173	0.052	0.173	0.047	0.170	0.051	0	0.991	-0.003	0.738	-0.003	0.707

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S3 Approximate entropy in the anterior-posterior direction as a function of *r* and *m* for a data length of *N*=600 (i.e. 30-seconds).

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	74.40	**<0.001**	0.619	0.106	0.676	0.095	0.678	0.112	0.057	**<0.001**	0.060	**<0.001**	0.003	0.949
0.15	88.83	**<0.001**	0.535	0.116	0.602	0.096	0.604	0.114	0.066	**<0.001**	0.068	**<0.001**	0.002	0.969
0.2	96.40	**<0.001**	0.457	0.123	0.530	0.101	0.532	0.121	0.073	**<0.001**	0.075	**<0.001**	0.002	0.979
0.25	99.33	**<0.001**	0.388	0.124	0.464	0.106	0.467	0.125	0.076	**<0.001**	0.079	**<0.001**	0.003	0.949
0.3	100.93	**<0.001**	0.331	0.119	0.405	0.107	0.409	0.124	0.075	**<0.001**	0.078	**<0.001**	0.003	0.924
0.35	101.02	**<0.001**	0.283	0.112	0.353	0.103	0.358	0.120	0.071	**<0.001**	0.075	**<0.001**	0.005	0.845
0.4	100.23	**<0.001**	0.243	0.102	0.308	0.098	0.314	0.114	0.065	**<0.001**	0.071	**<0.001**	0.006	0.744
0.45	98.87	**<0.001**	0.211	0.093	0.270	0.091	0.277	0.107	0.059	**<0.001**	0.066	**<0.001**	0.007	0.610
0.5	98.33	**<0.001**	0.185	0.084	0.238	0.083	0.246	0.099	0.053	**<0.001**	0.061	**<0.001**	0.008	0.488
m = 3														
0.1	70.06	**<0.001**	0.487	0.076	0.528	0.062	0.517	0.073	0.041	**<0.001**	0.030	**<0.001**	-0.010	0.148
0.15	94.52	**<0.001**	0.442	0.096	0.502	0.090	0.504	0.107	0.060	**<0.001**	0.062	**<0.001**	0.002	0.970
0.2	92.44	**<0.001**	0.388	0.096	0.446	0.090	0.452	0.108	0.058	**<0.001**	0.064	**<0.001**	0.006	0.689
0.25	93.34	**<0.001**	0.340	0.092	0.395	0.083	0.402	0.101	0.055	**<0.001**	0.061	**<0.001**	0.007	0.611
0.3	94.93	**<0.001**	0.300	0.088	0.353	0.078	0.359	0.095	0.053	**<0.001**	0.059	**<0.001**	0.006	0.648
0.35	97.34	**<0.001**	0.266	0.085	0.317	0.075	0.322	0.089	0.052	**<0.001**	0.056	**<0.001**	0.005	0.764
0.4	98.18	**<0.001**	0.237	0.082	0.286	0.072	0.290	0.085	0.050	**<0.001**	0.053	**<0.001**	0.004	0.836
0.45	98.11	**<0.001**	0.211	0.078	0.259	0.070	0.262	0.082	0.048	**<0.001**	0.051	**<0.001**	0.004	0.823
0.5	98.05	**<0.001**	0.189	0.074	0.234	0.067	0.238	0.078	0.045	**<0.001**	0.049	**<0.001**	0.004	0.783
m = 4														
0.1	8.86	**<0.001**	0.377	0.045	0.383	0.043	0.369	0.050	0.006	**0.011**	-0.007	0.070	-0.014	**<0.001**
0.15	94.50	**<0.001**	0.386	0.074	0.432	0.062	0.425	0.074	0.046	**<0.001**	0.039	**<0.001**	-0.007	0.440
0.2	101.23	**<0.001**	0.351	0.085	0.407	0.080	0.406	0.093	0.055	**<0.001**	0.055	**<0.001**	0	0.998
0.25	96.17	**<0.001**	0.313	0.085	0.366	0.081	0.370	0.096	0.053	**<0.001**	0.057	**<0.001**	0.004	0.825
0.3	93	**<0.001**	0.279	0.081	0.328	0.077	0.334	0.091	0.049	**<0.001**	0.055	**<0.001**	0.006	0.646
0.35	94.25	**<0.001**	0.249	0.077	0.295	0.072	0.301	0.085	0.047	**<0.001**	0.052	**<0.001**	0.006	0.602
0.4	95.30	**<0.001**	0.223	0.072	0.267	0.067	0.272	0.079	0.044	**<0.001**	0.049	**<0.001**	0.005	0.622
0.45	95.05	**<0.001**	0.201	0.068	0.243	0.063	0.248	0.074	0.041	**<0.001**	0.046	**<0.001**	0.005	0.635
0.5	95.07	**<0.001**	0.182	0.065	0.221	0.059	0.226	0.070	0.039	**<0.001**	0.044	**<0.001**	0.005	0.612
m = 5														
0.1	48.65	**<0.001**	0.276	0.048	0.256	0.056	0.245	0.064	-0.020	**<0.001**	-0.031	**<0.001**	-0.011	**0.022**
0.15	55.71	**<0.001**	0.324	0.049	0.348	0.037	0.336	0.045	0.023	**<0.001**	0.011	**0.002**	-0.012	**0.002**
0.2	101.59	**<0.001**	0.315	0.067	0.359	0.058	0.352	0.067	0.044	**<0.001**	0.037	**<0.001**	-0.007	0.363
0.25	100.98	**<0.001**	0.290	0.075	0.338	0.069	0.336	0.080	0.048	**<0.001**	0.047	**<0.001**	-0.001	0.966
0.3	94.79	**<0.001**	0.262	0.075	0.309	0.070	0.311	0.082	0.047	**<0.001**	0.049	**<0.001**	0.002	0.928
0.35	94.20	**<0.001**	0.236	0.072	0.281	0.068	0.285	0.080	0.044	**<0.001**	0.048	**<0.001**	0.004	0.774
0.4	94.45	**<0.001**	0.213	0.068	0.255	0.065	0.260	0.076	0.042	**<0.001**	0.046	**<0.001**	0.004	0.686
0.45	94.46	**<0.001**	0.193	0.064	0.233	0.061	0.237	0.072	0.039	**<0.001**	0.044	**<0.001**	0.005	0.623
0.5	94.15	**<0.001**	0.176	0.061	0.213	0.057	0.217	0.067	0.037	**<0.001**	0.042	**<0.001**	0.005	0.573

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S4 Approximate entropy in the medial-lateral direction as a function of *r* and *m* for a data length of *N*=600 (i.e. 30-seconds).

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	9.49	**<0.001**	0.641	0.092	0.631	0.085	0.613	0.089	-0.010	0.059	-0.028	**<0.001**	-0.018	**0.028**
0.15	4.57	**0.010**	0.564	0.097	0.560	0.089	0.543	0.099	-0.004	0.656	-0.021	**0.007**	-0.017	0.051
0.2	2.35	0.095	0.489	0.104	0.489	0.098	0.473	0.109	0	0.996	-0.016	0.087	-0.016	0.120
0.25	1.77	0.170	0.421	0.107	0.423	0.102	0.407	0.113	0.002	0.927	-0.013	0.210	-0.015	0.154
0.3	1.47	0.230	0.362	0.106	0.364	0.102	0.350	0.111	0.002	0.939	-0.012	0.274	-0.014	0.211
0.35	1.33	0.265	0.312	0.101	0.313	0.097	0.301	0.106	0.001	0.964	-0.011	0.298	-0.012	0.252
0.4	1.15	0.318	0.270	0.094	0.271	0.091	0.260	0.098	0.001	0.991	-0.010	0.329	-0.011	0.319
0.45	1.02	0.361	0.235	0.086	0.235	0.083	0.226	0.091	0	0.997	-0.009	0.363	-0.009	0.371
0.5	0.94	0.392	0.206	0.078	0.206	0.076	0.199	0.083	0	0.999	-0.008	0.377	-0.008	0.425
m = 3														
0.1	7.89	**<0.001**	0.497	0.065	0.492	0.068	0.477	0.072	-0.005	0.325	-0.020	**<0.001**	-0.015	**0.011**
0.15	7.34	**0.001**	0.457	0.082	0.449	0.079	0.434	0.083	-0.008	0.148	-0.023	**0.001**	-0.015	**0.046**
0.2	5.91	**0.003**	0.404	0.080	0.397	0.073	0.385	0.079	-0.007	0.164	-0.019	**0.003**	-0.012	0.112
0.25	3.91	**0.020**	0.358	0.076	0.354	0.069	0.343	0.076	-0.004	0.442	-0.015	**0.016**	-0.011	0.151
0.3	2.89	0.056	0.321	0.074	0.318	0.068	0.308	0.074	-0.003	0.759	-0.013	**0.043**	-0.010	0.153
0.35	2.13	0.119	0.287	0.072	0.286	0.066	0.276	0.073	-0.001	0.945	-0.011	0.100	-0.010	0.184
0.4	1.73	0.177	0.258	0.070	0.257	0.065	0.248	0.071	0	0.998	-0.009	0.166	-0.009	0.205
0.45	1.53	0.217	0.232	0.068	0.232	0.064	0.223	0.069	0	0.988	-0.008	0.227	-0.009	0.219
0.5	1.33	0.264	0.208	0.065	0.209	0.062	0.201	0.067	0.001	0.967	-0.007	0.294	-0.008	0.252
m = 4														
0.1	2.87	0.057	0.378	0.038	0.381	0.041	0.373	0.042	0.003	0.361	-0.005	0.268	-0.007	0.050
0.15	5.09	**0.006**	0.395	0.062	0.393	0.064	0.380	0.069	-0.002	0.761	-0.015	**0.004**	-0.013	**0.025**
0.2	5.28	**0.005**	0.362	0.073	0.357	0.071	0.345	0.075	-0.005	0.322	-0.017	**0.004**	-0.012	0.082
0.25	5.23	**0.005**	0.325	0.072	0.319	0.066	0.308	0.072	-0.006	0.222	-0.016	**0.005**	-0.011	0.130
0.3	4.68	**0.009**	0.292	0.068	0.286	0.061	0.277	0.066	-0.005	0.249	-0.014	**0.009**	-0.009	0.168
0.35	3.94	**0.020**	0.263	0.064	0.259	0.057	0.251	0.062	-0.004	0.352	-0.013	**0.018**	-0.008	0.193
0.4	3.25	**0.039**	0.239	0.060	0.235	0.054	0.228	0.059	-0.003	0.505	-0.011	**0.033**	-0.008	0.209
0.45	2.45	0.087	0.217	0.057	0.215	0.052	0.208	0.057	-0.002	0.730	-0.009	0.070	-0.007	0.232
0.5	1.90	0.150	0.198	0.055	0.197	0.050	0.190	0.055	-0.001	0.870	-0.008	0.125	-0.006	0.269
m = 5														
0.1	1.18	0.309	0.271	0.046	0.273	0.042	0.275	0.041	0.003	0.428	0.004	0.458	0.001	0.933
0.15	3.88	**0.021**	0.331	0.040	0.332	0.043	0.323	0.048	0.001	0.860	-0.008	**0.033**	-0.009	**0.017**
0.2	4.24	**0.014**	0.325	0.057	0.323	0.058	0.312	0.063	-0.002	0.702	-0.013	**0.010**	-0.010	0.059
0.25	4.02	**0.018**	0.299	0.064	0.296	0.062	0.286	0.066	-0.003	0.596	-0.013	**0.013**	-0.010	0.092
0.3	4.24	**0.015**	0.273	0.063	0.269	0.059	0.259	0.063	-0.004	0.376	-0.013	**0.012**	-0.009	0.145
0.35	4.20	**0.015**	0.248	0.061	0.243	0.055	0.235	0.060	-0.004	0.301	-0.012	**0.014**	-0.008	0.191
0.4	4	**0.018**	0.226	0.058	0.221	0.052	0.214	0.056	-0.004	0.282	-0.011	**0.019**	-0.007	0.236
0.45	3.21	**0.041**	0.206	0.054	0.203	0.048	0.196	0.053	-0.003	0.419	-0.010	**0.038**	-0.006	0.268
0.5	2.70	0.067	0.188	0.051	0.186	0.046	0.180	0.050	-0.003	0.541	-0.008	0.059	-0.006	0.288

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S5 Sample entropy in the medial-lateral direction as a function of *r* and *m* for a data length of *N*=1200 (i.e. 60-seconds).

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	0.91	0.403	0.615	0.138	0.619	0.125	0.605	0.131	0.004	0.831	-0.010	0.562	-0.014	0.370
0.15	1.26	0.283	0.476	0.119	0.484	0.109	0.472	0.115	0.008	0.358	-0.004	0.905	-0.012	0.410
0.2	1.45	0.236	0.384	0.110	0.392	0.102	0.382	0.107	0.008	0.257	-0.002	0.975	-0.010	0.453
0.25	1.40	0.247	0.316	0.100	0.324	0.094	0.315	0.098	0.008	0.265	-0.001	0.981	-0.009	0.476
0.3	1.21	0.297	0.265	0.090	0.272	0.086	0.264	0.089	0.006	0.321	-0.001	0.978	-0.008	0.513
0.35	1.04	0.355	0.226	0.080	0.231	0.077	0.224	0.080	0.005	0.386	-0.001	0.974	-0.006	0.550
0.4	0.88	0.416	0.194	0.071	0.198	0.068	0.193	0.072	0.004	0.453	-0.001	0.972	-0.005	0.592
0.45	0.74	0.476	0.169	0.063	0.173	0.061	0.168	0.064	0.003	0.509	-0.001	0.978	-0.004	0.644
0.5	0.64	0.530	0.149	0.057	0.152	0.054	0.148	0.058	0.003	0.559	-0.001	0.982	-0.004	0.689
m = 3														
0.1	1.30	0.273	0.551	0.143	0.555	0.136	0.537	0.141	0.004	0.870	-0.014	0.369	-0.018	0.243
0.15	0.92	0.397	0.420	0.107	0.423	0.099	0.412	0.103	0.003	0.811	-0.008	0.571	-0.011	0.364
0.2	0.84	0.433	0.343	0.090	0.347	0.082	0.339	0.086	0.004	0.660	-0.005	0.764	-0.008	0.442
0.25	0.92	0.397	0.290	0.081	0.295	0.073	0.288	0.077	0.004	0.513	-0.003	0.881	-0.007	0.479
0.3	0.96	0.384	0.250	0.074	0.255	0.068	0.249	0.071	0.004	0.445	-0.002	0.944	-0.006	0.528
0.35	0.97	0.379	0.218	0.068	0.222	0.063	0.217	0.065	0.004	0.426	-0.001	0.959	-0.005	0.545
0.4	0.93	0.396	0.192	0.063	0.196	0.059	0.191	0.061	0.004	0.437	-0.001	0.967	-0.005	0.568
0.45	0.87	0.420	0.170	0.058	0.174	0.055	0.169	0.056	0.003	0.454	-0.001	0.974	-0.004	0.599
0.5	0.79	0.456	0.152	0.054	0.155	0.051	0.151	0.052	0.003	0.488	-0.001	0.978	-0.004	0.630
m = 4														
0.1	1.64	0.194	0.525	0.145	0.532	0.139	0.512	0.143	0.007	0.589	-0.013	0.444	-0.020	0.175
0.15	1.23	0.292	0.398	0.108	0.402	0.102	0.389	0.106	0.004	0.739	-0.009	0.488	-0.013	0.262
0.2	0.94	0.389	0.324	0.089	0.326	0.082	0.317	0.085	0.003	0.778	-0.006	0.590	-0.009	0.360
0.25	0.70	0.495	0.274	0.076	0.276	0.069	0.269	0.073	0.003	0.763	-0.004	0.739	-0.007	0.482
0.3	0.66	0.519	0.237	0.068	0.239	0.061	0.234	0.064	0.003	0.709	-0.003	0.824	-0.006	0.534
0.35	0.65	0.524	0.208	0.062	0.211	0.056	0.206	0.059	0.003	0.659	-0.002	0.882	-0.005	0.572
0.4	0.65	0.525	0.185	0.057	0.187	0.052	0.183	0.054	0.003	0.615	-0.002	0.927	-0.004	0.609
0.45	0.62	0.537	0.165	0.053	0.167	0.048	0.164	0.050	0.002	0.598	-0.001	0.957	-0.004	0.651
0.5	0.59	0.556	0.148	0.049	0.151	0.045	0.148	0.047	0.002	0.600	-0.001	0.972	-0.003	0.686
m = 5														
0.1	1.88	0.153	0.501	0.142	0.509	0.137	0.489	0.140	0.008	0.443	-0.012	0.491	-0.020	0.151
0.15	1.44	0.238	0.382	0.106	0.387	0.101	0.373	0.105	0.005	0.640	-0.009	0.483	-0.014	0.216
0.2	1.20	0.301	0.312	0.087	0.315	0.0820	0.305	0.085	0.003	0.736	-0.007	0.503	-0.010	0.272
0.25	0.89	0.411	0.264	0.075	0.267	0.0690	0.259	0.072	0.003	0.769	-0.005	0.628	-0.008	0.385
0.3	0.71	0.491	0.229	0.067	0.231	0.0610	0.225	0.063	0.002	0.770	-0.004	0.727	-0.006	0.475
0.35	0.63	0.533	0.201	0.060	0.203	0.0540	0.198	0.057	0.002	0.759	-0.003	0.789	-0.005	0.529
0.4	0.54	0.581	0.179	0.055	0.181	0.0500	0.177	0.052	0.002	0.737	-0.002	0.866	-0.004	0.602
0.45	0.51	0.600	0.160	0.050	0.162	0.0460	0.159	0.047	0.002	0.708	-0.001	0.916	-0.003	0.650
0.5	0.46	0.634	0.144	0.047	0.146	0.0430	0.143	0.044	0.002	0.703	-0.001	0.953	-0.003	0.710

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S6 Sample entropy in the anterior-posterior direction as a function of *r* and *m* for a data length of *N*=600 (i.e. 30-seconds).

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	96.27	**<0.001**	0.622	0.165	0.724	0.156	0.737	0.187	0.102	**<0.001**	0.115	**<0.001**	0.013	0.565
0.15	107.59	**<0.001**	0.484	0.137	0.572	0.122	0.580	0.148	0.088	**<0.001**	0.096	**<0.001**	0.009	0.694
0.2	111.29	**<0.001**	0.394	0.124	0.476	0.112	0.481	0.133	0.082	**<0.001**	0.087	**<0.001**	0.005	0.871
0.25	111.62	**<0.001**	0.328	0.114	0.404	0.105	0.408	0.124	0.076	**<0.001**	0.080	**<0.001**	0.004	0.894
0.3	109.64	**<0.001**	0.277	0.104	0.347	0.099	0.351	0.116	0.070	**<0.001**	0.074	**<0.001**	0.004	0.896
0.35	107.43	**<0.001**	0.237	0.095	0.301	0.092	0.305	0.108	0.063	**<0.001**	0.067	**<0.001**	0.004	0.845
0.4	105.38	**<0.001**	0.206	0.085	0.262	0.085	0.267	0.099	0.057	**<0.001**	0.061	**<0.001**	0.005	0.787
0.45	103.19	**<0.001**	0.180	0.077	0.230	0.077	0.235	0.091	0.051	**<0.001**	0.056	**<0.001**	0.005	0.719
0.5	101.31	**<0.001**	0.159	0.069	0.204	0.070	0.209	0.083	0.045	**<0.001**	0.050	**<0.001**	0.005	0.667
m = 3														
0.1	98.14	**<0.001**	0.567	0.175	0.679	0.172	0.688	0.204	0.112	**<0.001**	0.121	**<0.001**	0.009	0.802
0.15	105.90	**<0.001**	0.432	0.132	0.519	0.131	0.531	0.158	0.087	**<0.001**	0.099	**<0.001**	0.012	0.508
0.2	106.88	**<0.001**	0.354	0.109	0.426	0.107	0.435	0.129	0.072	**<0.001**	0.081	**<0.001**	0.009	0.530
0.25	107.26	**<0.001**	0.300	0.095	0.362	0.091	0.369	0.110	0.062	**<0.001**	0.070	**<0.001**	0.007	0.579
0.3	107.27	**<0.001**	0.259	0.086	0.315	0.081	0.321	0.098	0.056	**<0.001**	0.062	**<0.001**	0.006	0.669
0.35	107.29	**<0.001**	0.226	0.079	0.278	0.074	0.282	0.088	0.052	**<0.001**	0.056	**<0.001**	0.004	0.780
0.4	106.56	**<0.001**	0.200	0.073	0.248	0.069	0.251	0.082	0.048	**<0.001**	0.052	**<0.001**	0.003	0.815
0.45	105.75	**<0.001**	0.178	0.068	0.222	0.065	0.225	0.076	0.045	**<0.001**	0.048	**<0.001**	0.003	0.820
0.5	103.89	**<0.001**	0.159	0.063	0.200	0.061	0.203	0.071	0.041	**<0.001**	0.044	**<0.001**	0.003	0.809
m = 4														
0.1	96.77	**<0.001**	0.538	0.176	0.651	0.174	0.657	0.205	0.113	**<0.001**	0.119	**<0.001**	0.006	0.909
0.15	107.22	**<0.001**	0.410	0.132	0.499	0.132	0.508	0.159	0.089	**<0.001**	0.098	**<0.001**	0.009	0.687
0.2	108.88	**<0.001**	0.336	0.108	0.410	0.109	0.417	0.132	0.074	**<0.001**	0.081	**<0.001**	0.007	0.685
0.25	106.78	**<0.001**	0.285	0.093	0.347	0.093	0.354	0.112	0.062	**<0.001**	0.070	**<0.001**	0.007	0.579
0.3	104.93	**<0.001**	0.247	0.082	0.301	0.081	0.308	0.098	0.054	**<0.001**	0.061	**<0.001**	0.007	0.566
0.35	104.19	**<0.001**	0.217	0.074	0.265	0.073	0.271	0.087	0.049	**<0.001**	0.054	**<0.001**	0.006	0.613
0.4	104.08	**<0.001**	0.192	0.068	0.237	0.066	0.241	0.078	0.044	**<0.001**	0.049	**<0.001**	0.005	0.644
0.45	103.50	**<0.001**	0.172	0.063	0.213	0.061	0.217	0.072	0.041	**<0.001**	0.045	**<0.001**	0.004	0.682
0.5	102.30	**<0.001**	0.155	0.058	0.192	0.056	0.196	0.066	0.038	**<0.001**	0.041	**<0.001**	0.004	0.693
m = 5														
0.1	75.78	**<0.001**	0.509	0.192	0.615	0.176	0.617	0.211	0.106	**<0.001**	0.109	**<0.001**	0.002	0.987
0.15	103.92	**<0.001**	0.389	0.128	0.475	0.128	0.480	0.152	0.086	**<0.001**	0.091	**<0.001**	0.005	0.874
0.2	107.87	**<0.001**	0.321	0.105	0.393	0.105	0.398	0.127	0.072	**<0.001**	0.077	**<0.001**	0.005	0.825
0.25	106.37	**<0.001**	0.274	0.091	0.335	0.091	0.341	0.109	0.061	**<0.001**	0.067	**<0.001**	0.006	0.703
0.3	104.62	**<0.001**	0.238	0.081	0.292	0.080	0.297	0.096	0.053	**<0.001**	0.059	**<0.001**	0.006	0.654
0.35	104.18	**<0.001**	0.210	0.073	0.258	0.072	0.263	0.086	0.048	**<0.001**	0.053	**<0.001**	0.005	0.647
0.4	103.06	**<0.001**	0.187	0.066	0.230	0.066	0.235	0.077	0.043	**<0.001**	0.048	**<0.001**	0.005	0.655
0.45	101.96	**<0.001**	0.168	0.061	0.207	0.060	0.211	0.070	0.039	**<0.001**	0.044	**<0.001**	0.004	0.652
0.5	100.66	**<0.001**	0.151	0.056	0.187	0.055	0.191	0.065	0.036	**<0.001**	0.040	**<0.001**	0.004	0.645

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S7 Sample entropy in the medial-lateral direction as a function of *r* and *m* for a data length of *N*=600 (i.e. 30-seconds).

	One-way ANOVA		Descriptive statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	4.27	**0.014**	0.658	0.145	0.651	0.133	0.627	0.139	-0.007	0.581	-0.031	**0.010**	-0.024	0.079
0.15	2.43	0.089	0.516	0.119	0.516	0.110	0.498	0.119	0	1	-0.019	0.083	-0.018	0.106
0.2	1.77	0.170	0.424	0.109	0.427	0.103	0.411	0.112	0.003	0.875	-0.013	0.234	-0.016	0.148
0.25	1.62	0.197	0.355	0.102	0.359	0.098	0.345	0.106	0.004	0.703	-0.010	0.367	-0.014	0.170
0.3	1.52	0.220	0.302	0.094	0.306	0.091	0.293	0.098	0.004	0.676	-0.009	0.423	-0.013	0.194
0.35	1.40	0.246	0.259	0.086	0.263	0.084	0.251	0.090	0.004	0.690	-0.008	0.456	-0.011	0.219
0.4	1.25	0.286	0.225	0.078	0.228	0.077	0.218	0.082	0.003	0.740	-0.007	0.479	-0.010	0.256
0.45	1.12	0.327	0.197	0.071	0.199	0.069	0.191	0.074	0.002	0.772	-0.006	0.511	-0.008	0.295
0.5	1.01	0.363	0.174	0.064	0.176	0.062	0.169	0.067	0.002	0.813	-0.005	0.527	-0.007	0.330
m = 3														
0.1	4.34	**0.013**	0.593	0.158	0.588	0.150	0.559	0.152	-0.006	0.743	-0.034	**0.009**	-0.029	**0.049**
0.15	3.71	**0.025**	0.453	0.115	0.448	0.107	0.430	0.111	-0.005	0.601	-0.023	**0.018**	-0.017	0.116
0.2	3.01	**0.049**	0.373	0.093	0.370	0.086	0.356	0.090	-0.003	0.733	-0.017	**0.038**	-0.013	0.147
0.25	2.29	0.101	0.318	0.082	0.317	0.075	0.305	0.079	-0.001	0.945	-0.013	0.085	-0.011	0.159
0.3	1.94	0.145	0.277	0.075	0.278	0.069	0.267	0.074	0	0.996	-0.010	0.146	-0.011	0.154
0.35	1.60	0.203	0.244	0.070	0.245	0.065	0.236	0.069	0.001	0.947	-0.008	0.239	-0.009	0.189
0.4	1.43	0.240	0.217	0.065	0.218	0.061	0.210	0.065	0.002	0.880	-0.007	0.321	-0.008	0.212
0.45	1.32	0.266	0.194	0.061	0.195	0.058	0.188	0.062	0.002	0.817	-0.006	0.395	-0.008	0.234
0.5	1.24	0.290	0.174	0.057	0.176	0.054	0.169	0.058	0.002	0.784	-0.005	0.452	-0.007	0.258
m = 4														
0.1	3.50	**0.030**	0.562	0.160	0.560	0.153	0.531	0.156	-0.002	0.980	-0.031	**0.026**	-0.029	**0.048**
0.15	3.37	**0.035**	0.428	0.117	0.424	0.110	0.405	0.115	-0.004	0.784	-0.022	**0.026**	-0.019	0.098
0.2	3.18	**0.042**	0.350	0.094	0.346	0.088	0.333	0.091	-0.004	0.673	-0.017	**0.032**	-0.013	0.147
0.25	2.86	0.058	0.298	0.080	0.295	0.073	0.284	0.077	-0.003	0.717	-0.014	**0.045**	-0.011	0.173
0.3	2.45	0.087	0.260	0.070	0.258	0.064	0.249	0.068	-0.002	0.825	-0.011	0.069	-0.009	0.190
0.35	2.14	0.118	0.230	0.064	0.229	0.058	0.220	0.062	-0.001	0.919	-0.010	0.098	-0.008	0.196
0.4	1.76	0.172	0.206	0.059	0.205	0.054	0.198	0.057	-0.001	0.975	-0.008	0.152	-0.007	0.228
0.45	1.48	0.228	0.185	0.055	0.185	0.050	0.179	0.053	0	1	-0.007	0.217	-0.007	0.255
0.5	1.29	0.276	0.168	0.051	0.168	0.047	0.162	0.050	0	0.993	-0.006	0.283	-0.006	0.280
m = 5														
0.1	2.58	0.076	0.529	0.160	0.530	0.157	0.504	0.160	0.001	0.991	-0.026	0.079	-0.027	0.081
0.15	2.92	0.054	0.406	0.113	0.403	0.108	0.385	0.114	-0.002	0.907	-0.020	**0.043**	-0.018	0.103
0.2	2.78	0.062	0.334	0.091	0.331	0.086	0.318	0.092	-0.003	0.758	-0.016	**0.048**	-0.013	0.167
0.25	2.70	0.067	0.285	0.078	0.283	0.073	0.272	0.077	-0.003	0.775	-0.013	0.053	-0.011	0.172
0.3	2.48	0.084	0.249	0.069	0.247	0.064	0.238	0.067	-0.002	0.827	-0.011	0.067	-0.009	0.183
0.35	2.29	0.102	0.221	0.062	0.219	0.057	0.211	0.060	-0.002	0.837	-0.010	0.082	-0.008	0.21
0.4	2.02	0.134	0.198	0.057	0.196	0.052	0.190	0.055	-0.001	0.862	-0.008	0.110	-0.007	0.249
0.45	1.66	0.190	0.179	0.052	0.178	0.048	0.172	0.051	-0.001	0.926	-0.007	0.163	-0.006	0.288
0.5	1.49	0.225	0.162	0.049	0.161	0.044	0.156	0.047	-0.001	0.965	-0.006	0.199	-0.005	0.301

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S8 Sample entropy in the anterior-posterior direction as a function of *r* and *m* for a data length of *N*=1200 (i.e. 60-seconds): eyes open – rigid surface (OR)

	One-way ANOVA		Summary statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	25.84	**<0.001**	0.540	0.156	0.640	0.157	0.662	0.190	0.100	**<0.001**	0.121	**<0.001**	0.022	0.663
0.15	30.58	**<0.001**	0.399	0.133	0.492	0.129	0.509	0.161	0.092	**<0.001**	0.109	**<0.001**	0.017	0.703
0.2	31.51	**<0.001**	0.310	0.118	0.394	0.117	0.411	0.148	0.084	**<0.001**	0.101	**<0.001**	0.017	0.628
0.25	31.25	**<0.001**	0.249	0.104	0.323	0.107	0.342	0.138	0.074	**<0.001**	0.093	**<0.001**	0.019	0.505
0.3	30.82	**<0.001**	0.204	0.091	0.269	0.096	0.288	0.127	0.064	**<0.001**	0.084	**<0.001**	0.020	0.405
0.35	30.26	**<0.001**	0.171	0.079	0.227	0.086	0.247	0.115	0.056	**<0.001**	0.075	**<0.001**	0.019	0.325
0.4	29.78	**<0.001**	0.146	0.070	0.195	0.077	0.214	0.104	0.049	**<0.001**	0.067	**<0.001**	0.019	0.264
0.45	29.52	**<0.001**	0.127	0.061	0.169	0.068	0.187	0.094	0.043	**<0.001**	0.060	**<0.001**	0.018	0.224
0.5	29.39	**<0.001**	0.111	0.054	0.149	0.061	0.165	0.085	0.038	**<0.001**	0.054	**<0.001**	0.016	0.196
m = 3														
0.1	24.08	**<0.001**	0.488	0.152	0.587	0.170	0.612	0.208	0.098	**<0.001**	0.124	**<0.001**	0.025	0.593
0.15	28.21	**<0.001**	0.363	0.114	0.442	0.127	0.463	0.155	0.079	**<0.001**	0.100	**<0.001**	0.021	0.538
0.2	30.17	**<0.001**	0.289	0.096	0.358	0.103	0.374	0.127	0.068	**<0.001**	0.085	**<0.001**	0.016	0.565
0.25	31.34	**<0.001**	0.238	0.086	0.300	0.089	0.314	0.112	0.062	**<0.001**	0.076	**<0.001**	0.014	0.569
0.3	32.03	**<0.001**	0.200	0.078	0.257	0.080	0.270	0.102	0.056	**<0.001**	0.069	**<0.001**	0.013	0.570
0.35	32.05	**<0.001**	0.171	0.071	0.222	0.073	0.235	0.094	0.051	**<0.001**	0.064	**<0.001**	0.012	0.538
0.4	31.88	**<0.001**	0.148	0.064	0.194	0.068	0.207	0.087	0.047	**<0.001**	0.059	**<0.001**	0.012	0.479
0.45	31.47	**<0.001**	0.129	0.059	0.171	0.062	0.184	0.081	0.042	**<0.001**	0.054	**<0.001**	0.012	0.421
0.5	31.06	**<0.001**	0.114	0.053	0.152	0.057	0.164	0.075	0.038	**<0.001**	0.050	**<0.001**	0.012	0.364
m = 4														
0.1	25.47	**<0.001**	0.463	0.151	0.566	0.171	0.588	0.214	0.103	**<0.001**	0.124	**<0.001**	0.022	0.684
0.15	28.46	**<0.001**	0.343	0.111	0.424	0.130	0.442	0.158	0.081	**<0.001**	0.099	**<0.001**	0.018	0.613
0.2	29.72	**<0.001**	0.275	0.092	0.341	0.103	0.358	0.127	0.066	**<0.001**	0.083	**<0.001**	0.017	0.530
0.25	30.52	**<0.001**	0.228	0.080	0.286	0.087	0.301	0.109	0.057	**<0.001**	0.073	**<0.001**	0.015	0.489
0.3	31.34	**<0.001**	0.194	0.071	0.245	0.076	0.258	0.096	0.051	**<0.001**	0.065	**<0.001**	0.013	0.504
0.35	31.83	**<0.001**	0.167	0.064	0.214	0.069	0.226	0.087	0.047	**<0.001**	0.059	**<0.001**	0.012	0.498
0.4	32.05	**<0.001**	0.145	0.059	0.188	0.062	0.200	0.079	0.043	**<0.001**	0.054	**<0.001**	0.011	0.486
0.45	32.04	**<0.001**	0.128	0.054	0.167	0.057	0.178	0.073	0.039	**<0.001**	0.050	**<0.001**	0.011	0.463
0.5	31.97	**<0.001**	0.113	0.050	0.150	0.053	0.160	0.067	0.036	**<0.001**	0.046	**<0.001**	0.010	0.435
m = 5														
0.1	24.20	**<0.001**	0.444	0.148	0.543	0.167	0.561	0.205	0.099	**<0.001**	0.116	**<0.001**	0.018	0.767
0.15	28.85	**<0.001**	0.331	0.109	0.410	0.126	0.428	0.156	0.079	**<0.001**	0.097	**<0.001**	0.018	0.605
0.2	29.91	**<0.001**	0.265	0.089	0.330	0.100	0.348	0.128	0.065	**<0.001**	0.083	**<0.001**	0.018	0.467
0.25	30.55	**<0.001**	0.221	0.078	0.277	0.086	0.294	0.109	0.056	**<0.001**	0.072	**<0.001**	0.016	0.425
0.3	31.29	**<0.001**	0.188	0.069	0.238	0.075	0.253	0.096	0.050	**<0.001**	0.064	**<0.001**	0.015	0.421
0.35	31.44	**<0.001**	0.163	0.062	0.208	0.067	0.221	0.085	0.045	**<0.001**	0.058	**<0.001**	0.013	0.426
0.4	31.80	**<0.001**	0.143	0.057	0.184	0.061	0.195	0.077	0.041	**<0.001**	0.053	**<0.001**	0.012	0.422
0.45	31.90	**<0.001**	0.126	0.052	0.163	0.055	0.175	0.070	0.037	**<0.001**	0.049	**<0.001**	0.011	0.389
0.5	32.05	**<0.001**	0.112	0.048	0.146	0.051	0.157	0.065	0.034	**<0.001**	0.045	**<0.001**	0.011	0.378

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S9 Sample entropy in the anterior-posterior direction as a function of *r* and *m* for a data length of *N*=1200 (i.e. 60-seconds): eyes closed – rigid surface (CR)

	One-way ANOVA		Summary statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	38.88	**<0.001**	0.542	0.167	0.673	0.157	0.694	0.212	0.131	**<0.001**	0.152	**<0.001**	0.021	0.706
0.15	44.38	**<0.001**	0.401	0.142	0.520	0.129	0.532	0.172	0.119	**<0.001**	0.132	**<0.001**	0.013	0.830
0.2	45.93	**<0.001**	0.312	0.125	0.421	0.119	0.433	0.153	0.108	**<0.001**	0.121	**<0.001**	0.012	0.807
0.25	46.09	**<0.001**	0.251	0.110	0.348	0.111	0.362	0.140	0.097	**<0.001**	0.111	**<0.001**	0.013	0.732
0.3	45.55	**<0.001**	0.207	0.096	0.293	0.103	0.307	0.127	0.086	**<0.001**	0.100	**<0.001**	0.014	0.649
0.35	44.90	**<0.001**	0.174	0.084	0.250	0.094	0.264	0.115	0.076	**<0.001**	0.090	**<0.001**	0.015	0.565
0.4	44.32	**<0.001**	0.149	0.074	0.215	0.085	0.230	0.103	0.066	**<0.001**	0.081	**<0.001**	0.014	0.492
0.45	43.86	**<0.001**	0.129	0.065	0.188	0.076	0.201	0.093	0.058	**<0.001**	0.072	**<0.001**	0.014	0.450
0.5	43.55	**<0.001**	0.114	0.057	0.165	0.069	0.178	0.083	0.052	**<0.001**	0.065	**<0.001**	0.013	0.418
m = 3														
0.1	36.82	**<0.001**	0.490	0.162	0.622	0.173	0.648	0.236	0.131	**<0.001**	0.157	**<0.001**	0.026	0.613
0.15	41.47	**<0.001**	0.365	0.123	0.469	0.128	0.488	0.174	0.104	**<0.001**	0.124	**<0.001**	0.019	0.610
0.2	43.70	**<0.001**	0.291	0.104	0.380	0.104	0.395	0.140	0.089	**<0.001**	0.104	**<0.001**	0.015	0.644
0.25	44.96	**<0.001**	0.240	0.092	0.320	0.090	0.332	0.120	0.079	**<0.001**	0.092	**<0.001**	0.012	0.682
0.3	45.53	**<0.001**	0.202	0.083	0.275	0.082	0.285	0.107	0.072	**<0.001**	0.083	**<0.001**	0.011	0.710
0.35	45.61	**<0.001**	0.173	0.075	0.239	0.076	0.249	0.097	0.066	**<0.001**	0.076	**<0.001**	0.010	0.682
0.4	45.09	**<0.001**	0.150	0.069	0.210	0.071	0.220	0.089	0.060	**<0.001**	0.070	**<0.001**	0.010	0.653
0.45	44.64	**<0.001**	0.132	0.062	0.186	0.066	0.196	0.082	0.055	**<0.001**	0.064	**<0.001**	0.010	0.619
0.5	44.23	**<0.001**	0.116	0.057	0.166	0.061	0.175	0.075	0.050	**<0.001**	0.059	**<0.001**	0.009	0.586
m = 4														
0.1	37.73	**<0.001**	0.466	0.162	0.602	0.175	0.623	0.244	0.136	**<0.001**	0.157	**<0.001**	0.021	0.720
0.15	41.48	**<0.001**	0.345	0.120	0.450	0.130	0.470	0.182	0.105	**<0.001**	0.125	**<0.001**	0.020	0.609
0.2	43.35	**<0.001**	0.277	0.099	0.364	0.105	0.380	0.143	0.087	**<0.001**	0.103	**<0.001**	0.016	0.594
0.25	44.04	**<0.001**	0.230	0.086	0.305	0.089	0.319	0.120	0.075	**<0.001**	0.089	**<0.001**	0.014	0.590
0.3	44.66	**<0.001**	0.196	0.077	0.262	0.078	0.274	0.104	0.067	**<0.001**	0.079	**<0.001**	0.012	0.607
0.35	44.78	**<0.001**	0.169	0.069	0.229	0.070	0.240	0.092	0.060	**<0.001**	0.071	**<0.001**	0.011	0.611
0.4	44.63	**<0.001**	0.147	0.063	0.202	0.064	0.212	0.083	0.055	**<0.001**	0.064	**<0.001**	0.009	0.634
0.45	44.14	**<0.001**	0.130	0.058	0.180	0.059	0.189	0.076	0.050	**<0.001**	0.059	**<0.001**	0.009	0.629
0.5	43.79	**<0.001**	0.116	0.053	0.162	0.055	0.170	0.070	0.046	**<0.001**	0.054	**<0.001**	0.008	0.615
m = 5														
0.1	38.93	**<0.001**	0.444	0.156	0.576	0.170	0.614	0.264	0.131	**<0.001**	0.170	**<0.001**	0.039	0.340
0.15	42.01	**<0.001**	0.332	0.116	0.434	0.126	0.455	0.183	0.102	**<0.001**	0.123	**<0.001**	0.021	0.552
0.2	44.02	**<0.001**	0.267	0.096	0.353	0.103	0.369	0.143	0.086	**<0.001**	0.102	**<0.001**	0.016	0.601
0.25	44.44	**<0.001**	0.223	0.083	0.296	0.087	0.310	0.119	0.073	**<0.001**	0.087	**<0.001**	0.014	0.589
0.3	44.47	**<0.001**	0.190	0.074	0.255	0.077	0.267	0.103	0.065	**<0.001**	0.077	**<0.001**	0.012	0.578
0.35	44.65	**<0.001**	0.165	0.067	0.223	0.069	0.234	0.091	0.058	**<0.001**	0.069	**<0.001**	0.011	0.574
0.4	44.20	**<0.001**	0.144	0.061	0.197	0.062	0.207	0.082	0.053	**<0.001**	0.062	**<0.001**	0.010	0.590
0.45	43.84	**<0.001**	0.128	0.056	0.176	0.057	0.185	0.074	0.048	**<0.001**	0.057	**<0.001**	0.009	0.599
0.5	43.36	**<0.001**	0.114	0.051	0.158	0.053	0.166	0.068	0.044	**<0.001**	0.052	**<0.001**	0.008	0.589

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S10 Sample entropy in the anterior-posterior direction as a function of *r* and *m* for a data length of *N*=1200 (i.e. 60-seconds): eyes open – foam surface (OF)

	One-way ANOVA		Summary statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	70.99	**<0.001**	0.585	0.131	0.708	0.108	0.754	0.142	0.123	**<0.001**	0.169	**<0.001**	0.046	**0.047**
0.15	76.61	**<0.001**	0.457	0.113	0.566	0.086	0.599	0.106	0.109	**<0.001**	0.142	**<0.001**	0.033	0.104
0.2	76.84	**<0.001**	0.369	0.106	0.471	0.080	0.499	0.094	0.102	**<0.001**	0.129	**<0.001**	0.027	0.165
0.25	76.30	**<0.001**	0.304	0.097	0.399	0.077	0.424	0.088	0.095	**<0.001**	0.120	**<0.001**	0.025	0.173
0.3	74.13	**<0.001**	0.254	0.088	0.340	0.073	0.364	0.084	0.086	**<0.001**	0.110	**<0.001**	0.024	0.163
0.35	72.06	**<0.001**	0.216	0.079	0.293	0.068	0.314	0.079	0.077	**<0.001**	0.099	**<0.001**	0.022	0.161
0.4	70.07	**<0.001**	0.186	0.071	0.254	0.063	0.274	0.073	0.069	**<0.001**	0.088	**<0.001**	0.020	0.155
0.45	68.05	**<0.001**	0.162	0.063	0.222	0.057	0.240	0.067	0.061	**<0.001**	0.079	**<0.001**	0.018	0.151
0.5	66.23	**<0.001**	0.142	0.056	0.196	0.052	0.212	0.061	0.054	**<0.001**	0.070	**<0.001**	0.016	0.159
m = 3														
0.1	68.71	**<0.001**	0.530	0.145	0.668	0.124	0.714	0.163	0.138	**<0.001**	0.184	**<0.001**	0.046	0.092
0.15	70.62	**<0.001**	0.408	0.109	0.514	0.097	0.552	0.126	0.106	**<0.001**	0.144	**<0.001**	0.039	0.056
0.2	71.92	**<0.001**	0.335	0.090	0.421	0.078	0.453	0.099	0.087	**<0.001**	0.118	**<0.001**	0.032	0.054
0.25	73.93	**<0.001**	0.282	0.079	0.359	0.066	0.385	0.084	0.077	**<0.001**	0.103	**<0.001**	0.026	0.067
0.3	74.18	**<0.001**	0.242	0.072	0.312	0.059	0.335	0.073	0.069	**<0.001**	0.092	**<0.001**	0.023	0.081
0.35	74.80	**<0.001**	0.211	0.066	0.275	0.054	0.295	0.066	0.064	**<0.001**	0.085	**<0.001**	0.020	0.094
0.4	74.31	**<0.001**	0.185	0.061	0.244	0.051	0.262	0.060	0.059	**<0.001**	0.078	**<0.001**	0.018	0.106
0.45	73.13	**<0.001**	0.163	0.057	0.218	0.048	0.234	0.056	0.055	**<0.001**	0.071	**<0.001**	0.017	0.118
0.5	71.51	**<0.001**	0.145	0.052	0.195	0.045	0.210	0.052	0.050	**<0.001**	0.066	**<0.001**	0.015	0.127
m = 4														
0.1	68.10	**<0.001**	0.510	0.144	0.647	0.121	0.688	0.158	0.136	**<0.001**	0.178	**<0.001**	0.042	0.133
0.15	70.46	**<0.001**	0.393	0.113	0.502	0.097	0.538	0.127	0.109	**<0.001**	0.145	**<0.001**	0.036	0.092
0.2	70.62	**<0.001**	0.321	0.093	0.411	0.081	0.441	0.103	0.090	**<0.001**	0.120	**<0.001**	0.031	0.076
0.25	71.45	**<0.001**	0.270	0.079	0.347	0.069	0.374	0.089	0.077	**<0.001**	0.104	**<0.001**	0.027	0.061
0.3	71.42	**<0.001**	0.233	0.070	0.300	0.061	0.324	0.077	0.067	**<0.001**	0.091	**<0.001**	0.024	0.060
0.35	72.06	**<0.001**	0.204	0.063	0.264	0.054	0.286	0.068	0.060	**<0.001**	0.082	**<0.001**	0.022	0.060
0.4	72	**<0.001**	0.180	0.057	0.235	0.049	0.254	0.061	0.055	**<0.001**	0.074	**<0.001**	0.019	0.068
0.45	71.81	**<0.001**	0.160	0.052	0.210	0.045	0.227	0.055	0.050	**<0.001**	0.068	**<0.001**	0.017	0.070
0.5	71.01	**<0.001**	0.143	0.048	0.189	0.042	0.205	0.050	0.046	**<0.001**	0.062	**<0.001**	0.016	0.076
m = 5														
0.1	69.61	**<0.001**	0.486	0.137	0.616	0.119	0.665	0.159	0.130	**<0.001**	0.180	**<0.001**	0.050	**0.047**
0.15	69.65	**<0.001**	0.379	0.110	0.484	0.093	0.520	0.125	0.105	**<0.001**	0.141	**<0.001**	0.036	0.075
0.2	70.31	**<0.001**	0.311	0.092	0.400	0.079	0.429	0.101	0.088	**<0.001**	0.117	**<0.001**	0.029	0.092
0.25	70.65	**<0.001**	0.264	0.079	0.340	0.068	0.366	0.089	0.076	**<0.001**	0.102	**<0.001**	0.026	0.078
0.3	70.41	**<0.001**	0.227	0.070	0.294	0.060	0.318	0.078	0.067	**<0.001**	0.091	**<0.001**	0.024	0.062
0.35	70.12	**<0.001**	0.199	0.062	0.259	0.054	0.28	0.069	0.060	**<0.001**	0.081	**<0.001**	0.021	0.062
0.4	70.06	**<0.001**	0.176	0.056	0.230	0.049	0.249	0.061	0.054	**<0.001**	0.073	**<0.001**	0.019	0.070
0.45	69.37	**<0.001**	0.157	0.051	0.206	0.045	0.223	0.055	0.049	**<0.001**	0.066	**<0.001**	0.017	0.070
0.5	68.61	**<0.001**	0.141	0.047	0.185	0.041	0.201	0.050	0.045	**<0.001**	0.060	**<0.001**	0.016	0.076

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences

Table S11 Sample entropy in the anterior-posterior direction as a function of *r* and *m* for a data length of *N*=1200 (i.e. 60-seconds): eyes closed – foam surface (CF)

	One-way ANOVA		Summary statistics by group						Post-hoc					
			Young (Y)		Non-Fallers (NF)		Fallers (F)		NF - Y		F - Y		F - NF	
r	**F**	**p-value**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**MD**	**p-value**	**MD**	**p-value**	**MD**	**p-value**
m = 2														
0.1	20.34	**<0.001**	0.667	0.142	0.738	0.111	0.764	0.148	0.071	**<0.001**	0.097	**<0.001**	0.026	0.435
0.15	23.51	**<0.001**	0.532	0.111	0.591	0.085	0.610	0.110	0.060	**<0.001**	0.079	**<0.001**	0.019	0.483
0.2	25.31	**<0.001**	0.440	0.100	0.497	0.079	0.512	0.097	0.057	**<0.001**	0.072	**<0.001**	0.015	0.585
0.25	25.36	**<0.001**	0.371	0.093	0.425	0.076	0.437	0.091	0.054	**<0.001**	0.066	**<0.001**	0.013	0.638
0.3	24.61	**<0.001**	0.315	0.086	0.365	0.073	0.377	0.087	0.050	**<0.001**	0.061	**<0.001**	0.012	0.653
0.35	23.83	**<0.001**	0.271	0.079	0.316	0.068	0.327	0.081	0.045	**<0.001**	0.056	**<0.001**	0.011	0.646
0.4	22.97	**<0.001**	0.235	0.072	0.276	0.064	0.286	0.075	0.041	**<0.001**	0.051	**<0.001**	0.010	0.617
0.45	22.15	**<0.001**	0.206	0.065	0.242	0.058	0.252	0.069	0.036	**<0.001**	0.046	**<0.001**	0.010	0.594
0.5	21.49	**<0.001**	0.182	0.059	0.214	0.053	0.223	0.062	0.032	**<0.001**	0.041	**<0.001**	0.009	0.572
m = 3														
0.1	20.78	**<0.001**	0.615	0.158	0.697	0.124	0.717	0.161	0.082	**<0.001**	0.103	**<0.001**	0.020	0.667
0.15	21.93	**<0.001**	0.476	0.120	0.540	0.099	0.561	0.127	0.064	**<0.001**	0.085	**<0.001**	0.021	0.487
0.2	21.92	**<0.001**	0.394	0.097	0.445	0.080	0.463	0.102	0.051	**<0.001**	0.070	**<0.001**	0.018	0.423
0.25	22.99	**<0.001**	0.336	0.082	0.380	0.068	0.396	0.086	0.044	**<0.001**	0.060	**<0.001**	0.016	0.405
0.3	22.99	**<0.001**	0.292	0.073	0.332	0.061	0.345	0.075	0.040	**<0.001**	0.053	**<0.001**	0.013	0.466
0.35	23.28	**<0.001**	0.257	0.066	0.293	0.056	0.304	0.068	0.037	**<0.001**	0.047	**<0.001**	0.011	0.528
0.4	23.12	**<0.001**	0.228	0.061	0.261	0.052	0.271	0.062	0.034	**<0.001**	0.044	**<0.001**	0.010	0.534
0.45	23	**<0.001**	0.203	0.056	0.234	0.049	0.243	0.058	0.031	**<0.001**	0.040	**<0.001**	0.009	0.560
0.5	22.90	**<0.001**	0.182	0.052	0.211	0.046	0.219	0.054	0.029	**<0.001**	0.037	**<0.001**	0.008	0.570
m = 4														
0.1	21.36	**<0.001**	0.592	0.151	0.671	0.119	0.693	0.159	0.079	**<0.001**	0.101	**<0.001**	0.022	0.604
0.15	22.49	**<0.001**	0.461	0.121	0.527	0.097	0.543	0.125	0.066	**<0.001**	0.082	**<0.001**	0.016	0.663
0.2	22.47	**<0.001**	0.380	0.101	0.434	0.083	0.450	0.104	0.055	**<0.001**	0.070	**<0.001**	0.015	0.581
0.25	23.09	**<0.001**	0.322	0.085	0.369	0.071	0.384	0.089	0.047	**<0.001**	0.061	**<0.001**	0.015	0.505
0.3	22.70	**<0.001**	0.280	0.074	0.320	0.063	0.333	0.078	0.040	**<0.001**	0.053	**<0.001**	0.013	0.491
0.35	22.55	**<0.001**	0.246	0.065	0.282	0.057	0.293	0.069	0.036	**<0.001**	0.047	**<0.001**	0.011	0.519
0.4	22.37	**<0.001**	0.219	0.059	0.251	0.051	0.261	0.062	0.032	**<0.001**	0.042	**<0.001**	0.010	0.500
0.45	22.18	**<0.001**	0.197	0.053	0.226	0.047	0.235	0.056	0.029	**<0.001**	0.038	**<0.001**	0.009	0.499
0.5	22.19	**<0.001**	0.177	0.049	0.204	0.044	0.212	0.051	0.027	**<0.001**	0.035	**<0.001**	0.009	0.495
m = 5														
0.1	21.71	**<0.001**	0.560	0.143	0.636	0.116	0.660	0.156	0.076	**<0.001**	0.100	**<0.001**	0.024	0.514
0.15	22.43	**<0.001**	0.444	0.115	0.507	0.092	0.523	0.122	0.063	**<0.001**	0.079	**<0.001**	0.016	0.623
0.2	22.55	**<0.001**	0.368	0.098	0.422	0.080	0.436	0.102	0.054	**<0.001**	0.068	**<0.001**	0.014	0.609
0.25	23.24	**<0.001**	0.314	0.084	0.361	0.070	0.373	0.088	0.047	**<0.001**	0.059	**<0.001**	0.012	0.600
0.3	23.32	**<0.001**	0.273	0.074	0.314	0.062	0.325	0.077	0.041	**<0.001**	0.052	**<0.001**	0.011	0.587
0.35	23.09	**<0.001**	0.240	0.065	0.277	0.057	0.286	0.068	0.037	**<0.001**	0.046	**<0.001**	0.010	0.608
0.4	22.76	**<0.001**	0.214	0.058	0.247	0.052	0.255	0.061	0.033	**<0.001**	0.041	**<0.001**	0.009	0.597
0.45	22.27	**<0.001**	0.192	0.053	0.221	0.047	0.230	0.056	0.029	**<0.001**	0.038	**<0.001**	0.008	0.569
0.5	21.98	**<0.001**	0.174	0.048	0.200	0.044	0.208	0.051	0.026	**<0.001**	0.034	**<0.001**	0.008	0.543

F F-statistic, *SD* standard deviation, *MD* mean difference
Bold values indicate significant differences